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VETERINARY MEDICINE

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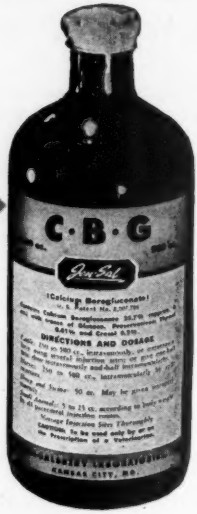

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D. M. CAMPBELL, *Editor*
7632 S. Crandon Ave., Chicago 49, Ill.
Telephone South Shore 7160

H. J. MOSTYN, *Eastern Representative*
P. O. Box 391, Dover, New Jersey
Telephone Dover 6-2711W.

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Anaplasmosis is being reported in new territory every year and is fast becoming a disease of major importance.—L. R. VAWTER.

In 1904 there were fewer than 10,000 hospital beds for the tuberculous in the United States. Today there are 100,000, but 40,000 more are needed.—*National Tuberculosis Association.*

A blood coagulation test for cancer was announced at the recent meeting of the American Association for Cancer Research at Atlantic City. The test is so simple that, if further study confirms its value, it is suitable for mass screening of populations.

The Tennessee Department of Public Health held portions of a shipment of Illinois cheese, that caused 250 cases of food poisoning, for a period of 302 days at temperatures ranging from 43° to 48° F. At the end of that period it still contained viable *Salmonella typhimurium.*

Promin, diasone and promizole, three sulfone compounds, have proved the most effective drugs so far used at the Carville Leprosarium. Practically 100% of even advanced cases of leprosy have been arrested by treatment extending over a period of three years. Improvement began as early as six months after treatment was initiated in 25% of the patients. In a year 60% were improved, and in two years 75% of the cases were arrested.

During World War II there were more persons killed in accidents on the home front than were killed on the battle front.

Mortality among laying hens in 1946 was about 17.4%. Of this total, leucosis is estimated to have been responsible for almost 40%.

When all factors involved are considered, it is estimated that the cost of the common cold to the American people is well over a billion dollars a year.

With the sole exception of bacterial diseases of dairy cattle, the diseases of farm animals caused by parasitic worms are of greater economic importance than are any other group of diseases with which the husbandman has to contend.—E. L. TAYLOR in *Vet. Rec.*

The Pitman-Moore Company announces the development of a new vaccine for the prevention of distemper in mink. The vaccine is a ferret spleen emulsion. The novelty in connection with the new vaccine is inactivation by exposure to ultraviolet light instead of to formaldehyde.

Marlate methoxychlor is the name of a new insecticide, manufactured by E. I. du Pont de Nemours & Co., which is said to kill a large variety of insect pests of domestic animals and plants. It is as non-toxic as rotenone and has a long lasting residual effect. It may be used as a dust, spray or dip.

Veterinary Corps Officers Separated from the Service Since VE-Day

(Supplemental to lists previously published)

Alabama
Davis, James J.
Arkansas
Corley, Glenn P.
California
Crane, Charles S.
Colorado
Brown, William W — Starkebaum, C. C.
Connecticut
Greer, Russell F.
Georgia
Derrick, Jesse D
Illinois
Gooch, John M. — Sedlacek, Glen E.
Iowa
Griswold, David M. — Kleveland, R. C.
McCracken, D. D. — Wehler, Duane R.
Kansas
Dehner, Lorid A. — Keith, Richard M.
Louisiana
Rodriguez, E. F., Jr.
Michigan
Godisak, John J. — Grossman, Samuel M.
Zingeser, E. R.
Missouri
Mahnken, Keith W. — Morley, William J.
Nebraska
Emery, Rex W — Hittle, Harold E.
Nisley, Bryant B.
New Jersey
Ellmers, George A.
New York
Holden, Chester J. — McEntee, Kenneth
Sayres, Joseph P.
North Dakota
Clark, Delbert D.
Ohio
Duncan, Charles S. — Hall, R. L., Jr.
Walker, James M. — McKenzie, Carl V.
Oklahoma
Cochran, Albert B.
Pennsylvania
Espy, George E. — Krechmer, Morton B.
Slider, Howard B.
Texas
Banks, William C. — Kelly, R. J., Jr.
Wisconsin
Petersen, Floyd N.
Wyoming
Sheppard, Asa N.

Officers Returned to Active Service:

Capt. Omar G. Werntz, 5035th ASU Chicago, w/sta at Des Moines. Iowa.
Major Wilson M. Osteen, Pomona QM Depot, Pomona, Calif.
Major Clifford W. Turner, 6003d ASU, Fort Ord, Calif.
Capt. Emmanuel F. Coyle, 1101st ASU Boston, w/sta at Worcester, Mass.
Capt. Harold D. Valentine, Bergstrom Field, Austin, Texas.
Capt. Dwain T. Bowie, Chicago QM Depot, Chicago, Ill.
Lt. Col. Merrill L. Steele, 4005th ASU, Camp Hood, Texas.
Major Elwin R. Prather, 5022nd ASU, Camp Carson, Colo.
Major Victor J. Cook, 2505 AFBU, Scott Field, Belleville, Ill.

Only about 50% of the government veterinary positions in the U. S. Zone in Germany are filled by permanent appointees, because of unavailability of politically and technically qualified specialists. Courses of instruction have been organized by the Veterinary Section of the Military Government to prepare veterinarians for these positions, which are now held by temporary appointees.

Veterinarian Indiana's Man of the Year

Dr. Leslie M. Hutchings, Associate Pathologist on the veterinary research staff of Purdue University, was recognized as Indiana's outstanding young man of 1947 at the annual Mid-Year Conference of the Indiana Junior Chamber of Commerce, January 24, 1948. Doctor Hutchings is recognized as the nation's leader in the field of swine brucellosis, one of the principal sources of undulant fever in persons.

President of the Hoosier young men's organization, O. H. Roberts, of Evansville said: "The Indiana Junior Chamber of Commerce makes this award to the young man, selected by a distinguished panel of leaders in government, medicine, business, agriculture and education, who in their opinion made the outstanding contribution in his field of endeavor and who by his work and other activities has contributed most to the general welfare of Indiana and its people during 1947."

Lieutenant Governor Richard T. James, chairman of the judging committee, in making the presentation of the key to Dr. Hutchings, stated: "Here is a young man, just 32 years old, who has this year successfully conducted research making possible, for the first time, a practical answer for the control of a disease that a State Commissioner of Health estimated effects 350,000 or 10 percent of our state's population. In conducting this research Doctor Hutchings has exposed himself and contracted undulant fever which continues to cause his confinement periodically. The successful research in brucellosis in swine is not only of vast economic importance to the swine industry but also to the health of our state and national, rural population. Also as a result of his work, Doctor Hutchings is now recognized as the outstanding authority in this nation on the public health aspects of brucellosis. Competent available data from public health departments, all over the country, indicate that approximately 70% of those suffering from undulant fever, are effected with the type of the disease that Doctor Hutchings has been studying with productive result. Thus, a young man has made another outstanding contribution in his field affecting many."

Senior veterinary medical students at the University of Pennsylvania School of Veterinary Medicine listening to description of the methods employed in the preparation of Sharp and Dohme rabies vaccine (veterinary). Eight faculty members and 38 students recently visited the Company's biological and research laboratories in Glenolden, Pennsylvania.

In the establishment of military governments in occupied countries following cessation of hostilities, veterinary service was given an important place in plans for getting livestock production re-established. Significantly, for the first time in history animal plagues did not sweep across the defeated nations following war and become a prime factor in the famine and general chaos as has been the case in all previous major wars.

There is an adequate number of veterinary practitioners in the U. S. Zone in Germany. However, because of past Nazi activities not all are permitted to practice. Of 741 veterinary practitioners in Bavaria, 24 are not permitted to practice; of 204 in Wuerttemberg practice is proscribed for 32, and of 411 in Hesse 24 (of whom 12 are still prisoners of war) may not practice. The total veterinary population of the U. S. Zone is 2011.

Beginning in 1949-50, two years of college preparation will be required for entrance to the New York State Veterinary College at Cornell University, Dean W. A. Hagan has announced. The current requirement is one year of college preparation, but the future two years' requirement will permit the student to obtain a more complete basic education before beginning his professional veterinary training. In his preparatory work "in an approved college or university," the student will be required to complete six semester hours each in English, physics, and biology or zoology, and 12 semester hours of chemistry.

To understand the future, one must be in possession of the essential facts of the past.—*Surgeon General Bliss.*

The problem of rabies control is a problem of dealing with human beings. Its solution is one part science and 99 parts human relations. —*Zeissig.*

The Santa Gertrudis strain of cattle, developed by the famous King Ranch in South Texas will be given a feeding test at the West Texas experiment station near Balmorhea. The Santa Gertrudis strain is five-eighths Shorthorn and three-eighths Brahma. It inherits the heat and insect tolerance of the latter and the "beefiness" of the Shorthorn.

Institute of Animal Physiology to Be Set Up

The British Agricultural Research Council has decided, after a careful review, that in many directions progress toward the improvement of animal health and production is restricted by lack of knowledge of the fundamental physiology of farm animals. To fill in some of the gaps in knowledge a new Institute of Animal Physiology is needed, and the British Ministry of Agriculture has decided to establish this. The director will be Professor I. de Burgh Daly, who is professor of physiology in Edinburgh University. It is hoped that he will take office early in 1948. The council proposes to appoint as his senior colleagues two scientific workers of high distinction in biochemistry and pathology.—*J. Am. Med. Assn.* 135:7, p. 447. 1948.

Foot-and-Mouth Disease Quarantine Line Pushed Back

A 100-mile section of the northern quarantine line maintained in central Mexico against foot-and-mouth disease has been moved southward as much as 50 miles in some places, following inspections which indicate that no infections exist in the area. The change in the quarantine line is in the State of San Luis Potosi.

In addition to the pushing back of a part of the northern quarantine line, several areas of infection nearest the quarantine line in the State of Veracruz have been freed of the disease. During the entire campaign no case of the foot-and-outh disease has appeared north of the present quarantine line.

Other developments in the campaign against foot-and-mouth disease are:

Construction of a 90-mile section of fence is under way near the eastern part of the northern quarantine line to give added protection to the line in that area. Engineering crews with bulldozers have completed clearing for the fence through 30 miles of jungle and swampy terrain.

A program of vaccination in the northern buffer zone is getting under way. (The buffer zones are areas that lie between the main infected area and the northern and southern quarantine lines.) The vaccine is being used first to protect healthy animals in areas where infection has occurred within or near the zone. Thus far the supply of vaccine is limited.

Vaccination Gets Slow Start

In November 1947 the decision was reached to supplant slaughter as a method of foot-and-mouth disease eradication in Mexico with vaccination; slaughter and burial being restricted to the north and south quarantine lines buffer zones and free territory should any outbreaks occur in it. It was not till late February that vaccination could begin and 25,000 doses were used in the northern buffer zone. To March 18th 58,000 doses of vaccine had been received from Argentina and 25,000 from the Netherlands. For effective use in the infected area millions of doses will be required.

The Bureau would like to establish its foot-and-mouth disease research laboratory at the eastern tip of Long Island, New York. The livestock interests of the state are being consulted as to their attitude toward the project. Over the years livestock raisers have been told repeatedly that foot-and-mouth disease research cannot be conducted without danger of the spread of the disease to susceptible livestock in the vicinity. Now when it is desirable to initiate such research, livestock interests are skeptical of assurances that the research does not constitute an important hazard.

Dr. H. W. Schoening, chief of the Pathological Division of the Bureau, recently visited various foot-and-mouth disease research centers in Europe to determine how escape of the infection from such centers is prevented. At Pirbright, England, reliance is placed solely on sanitary measures, and although cattle are maintained in the vicinity of the laboratory there has been no escape of the infection in the 25 years that research has been conducted at that institution.

At the foot-and-mouth disease vaccine laboratory at the Beringwerke, Warburg, Land Hesse, Germany, while quarantine and sanitation are of course employed, main reliance for preventing escape of the virus is placed on vaccination every six months of all cloven hoofed animals in the vicinity.

The Veterinary Section of the Military Government of the U. S. Zone in Germany has been remarkably successful in the control of foot-and-mouth disease in that area. Early in 1946 the number of newly infected farms per fortnight reached 240. By September the outbreak was suppressed, but it flared up again in November. In the first two weeks in December 75 new centers of infection were discovered. By the middle of January 1947 new centers of infection were reduced to five per week and since April 1947 none have occurred.

The Vaccine Situation

The United States has agreed to give Mexico all possible technical help in the development of vaccine for foot-and-mouth disease. The Mexican Government in turn has named a consultant board of five eminent Mexican scientists to supervise a research and vaccine-development program. Existing laboratory facilities of the Mexican Government in Mexico City are being remodeled and enlarged in preparation for this work.

The British laboratory at Pirbright, England, has identified eight lots of virus from Mexico; all being variants of type A.

U. S. Employe Killed

Although the cattlemen in the section of Mexico crossed by the northern quarantine line take more kindly to the work of the U. S.-Mexico Commission on foot-and-mouth disease than did residents of the infected zone and in fact a majority actively support the work, some individuals resent and obstruct all activities in connection with the work. Such opposition resulted in the death of one of the U. S. employees, September 28, 1947, from a shotgun wound. Work has been discontinued in the section where the killing occurred until the Mexican army can guarantee the safety of U. S. citizens.

B. A. I. Veterinarians Engage in Foot-and-Mouth Research in Europe

To obtain first-hand information on foot-and-mouth disease research in Europe and methods used for the prevention and control of the disease in different countries, the US DA has sent three research workers abroad for study. Dr. L. O. Mott, Dr. H. W. Johnson, and Dr. E. A. Eichhorn, of the Pathological Division of the Department's Bureau of Animal Industry, make up this team. They will engage in cooperative work with investigators in various research institutions, where they will have the opportunity to become familiar with facilities and procedures used and the problems encountered in foot-and-mouth disease research. The three United States scientists arrived in Europe about the middle of March and began their studies at the British foot-and-mouth disease research laboratory at Pirbright. Later they will proceed, as a group or individually, to laboratories in Holland, Denmark, Switzerland and possibly other countries.

Their work is a part of a program of research designed to obtain, quickly, information useful for increasing the protection of the livestock industry of the United States against the disease. The same knowledge will be available also for furthering control of the disease in Mexico.

The studies to be pursued by the United States scientists in Europe cover four principal projects. One is the study, through animal experimentation and sero-logical means, of the various types of foot-and-mouth disease virus. Another project deals with the methods of preparing and testing vaccines, made from Mexican and European strain of viruses.

A third project involves procedures for diagnosing the disease. And the fourth consists of investigations of the chemical, physical, immunological, and other properties of the viruses. In the work outlined, the experimental animals used will include cattle, swine, and guinea pigs. The duration of the assignment depends both on the rate of progress made and needs that may develop with respect to research work in Mexico and United States, all of which are to be closely integrated.

The work of the three American veterinarians, as outlined, is being conducted under authority granted the Secretary of Agriculture to combat foreign diseases, dangerous to the United States with particular reference to the outbreak of foot-and-mouth disease in Mexico. Recognizing a need also for fundamental research on foot-and-mouth disease, Department officials have also proposed a long-time program conducted within the United States.

A St. Louis Veterinary College

In volume 10 (last six months, 1862), page 168, of the *Prairie Farmer* it is stated: "Dr. Geo. H. Dadd is now in Chicago with the object of making arrangements for a permanent location here for the practice of veterinary surgery etc. and will probably open a school of instruction similar to the one he established in St. Louis."

There appears to be no mention in veterinary literature of a veterinary school in St. Louis. It is well known of course that Dadd was associated with Slade, Wood, and Copeman in the Boston Veterinary Institute (1854-57) and that he established and conducted the Chicago Veterinary Institute (1863-68). The first class at the latter institution was graduated in January 1864. It comprised J. H. Judson, Palo, Illinois, and G. T. Otis, Chicago. It is stated that this class saw more than 300 cases in the clinic (Dadd's practice).

Maintaining the Strength of Arsenic Dips

One problem in the use of arsenical dips has been oxidation—changing of the arsenious to an arsenic acid or of the trioxide to the pentoxide. The latter is much less active as a parasiticide than the trioxide, and to keep up the strength of the solution in the dipping vat it has been customary to add arsenic trioxide from time to time. This has sometimes resulted in poisoning animals, particularly sheep, which were dipped in these solutions of uncertain strength.

Recent experimentation in Australia has discovered that the addition of two gallons of cane molasses to 400 gallons of arsenic dip at intervals of six months prevents oxidation of the arsenious acid and maintains the strength of the solution indefinitely, under Australian conditions. Where oxidation has already taken place the molasses will reverse the process and restore the strength of the dipping solution.

In view of the convenience, safety, and effectiveness of the comparatively harmless DDT spray for animals, there is little occasion for using the dangerous arsenic dips for ticks, mites or lice.

That the rodent poison 1080 (sodium monofluoracetate) is toxic to chickens has been reported by Dr. L. H. Schwarte, Iowa State College. Five milligrams of the poison per kilogram of body weight caused symptoms of poisoning and 14 milligrams caused death of the birds.

Scientists at the University of Chicago have discovered that if the air in schools, theaters and offices has a relative humidity of 50%, airborne disease germs can be checked. This amount of humidity was found to be lethal to Type I pneumococci, staphylococci, and streptococci, but the humidity must be exact for the germs studied survive for long periods at higher or lower relative humidity. The studies were made at approximately 72°F.; at higher or lower temperatures the result from 50% humidity are not so effective.

Q Fever Virus in Raw Milk

Scientists of the U. S. Public Health Service have found Q fever virus in raw milk but so far they have not been able to find that the disease is transmitted through drinking milk. However, there have been outbreaks of the disease mainly among stock handlers, packing house and stockyard workers. Of extensive outbreaks in five California counties last spring in which there were 117 cases, more than one-half of the patients lived near or worked in dairies. In a survey it was found that from one-tenth to one-fifth of the dairy cows in Los Angeles County had Q fever antibodies in their blood. The testing of raw milk for Q fever was instituted because of these findings. Much study on the subject will be necessary.

Add Polymyxin to Antibiotic Agents

A new antibiotic agent developed independently from soil bacteria by research workers at the USDA Regional Research Laboratory at Peoria, Illinois, and at the American Cyanamid Company has been named polymyxin. It has received a limited clinical trial at Johns Hopkins Medical School at Baltimore where it made an impressive showing against certain gram negative disease organisms; being from 25 to 1000 times as effective as streptomycin against most gram negative germs. It is not, however, effective again *Mycobacterium tuberculosis*. Preliminary trials have raised expectations that it will be more effective than any other known treatment for brucellosis, tularemia, bacillary dysenterias, para-typhoid infections, etc.

The use of promizole with streptomycin saved six of seven babies and children suffering from tuberculous meningitis, as reported by Bellevue Hospital of New York University. The use of the two together heightens the action of the two remedies beyond the expected value of either alone. Although cases have been reported of excessive nerve damage by streptomycin, when the combined drugs were used these patients had no symptoms of nerve damage except mild ones in two cases.

A "mysterious" disease of wild muskrats, thought by some to be distemper, is reported by the state game director to have reduced the muskrat population of the principal Maryland marshes by 50% in the past three years. The disease is said to be more prevalent at present than at any time heretofore. Some trappers blame loss of muskrats on raccoons, but it is not known that this animal kills muskrats. Other trappers blame foxes.

Runnymede Farms in the San Fernando valley, California, claims to be the largest poultry farm in the world. It comprises 120 acres, largely occupied by poultry houses. The chickens number about 600,000. Two hundred sixty employees, 160 of whom live in dormitories on the farm, are required to operate it. All employees work eight hours a day, six days a week. The hatchery has a capacity for 800,000 eggs; the brooding plant a capacity of 158,000 chicks and the pullet battery plant capacity for 135,000 growing pullets.

Attacks on Viruses and Rickettsial

The spectacular results from chemotherapy and antibiotic therapy in certain bacterial, spirochetal and protozoan diseases has no analogue among virus or rickettsial diseases. That the course of this latter group of diseases is unaffected by any known chemical or antibiotic agent is believed to be due to differences in the metabolism of these two groups of pathogenic organisms. This belief has led many to the conclusion that the discovery of a chemical or antibiotic agent that would kill ,or arrest the multiplication of, viruses and rickettsiae is improbable.

Recent research justifies a more optimistic view. Meicklejohn reports penicillin-sulfadiazine therapy has some value in psittacosis. Experimental rickettsial infections have been reported by Grieff to be susceptible to some degree, to penicillin; while he and Snyder *et al.* have shown that para-aminobenzoic acid has an inhibiting effect on Rickettsia, and nitroacridine has a similar effect on influenza virus B when inoculated into chick embryos.

A Side Line for Veterinarians

Dr. C. R. Corson and Dr. W. H. House, two young Middlebury, Indiana, veterinarians, are engaged in a novel enterprise which they conduct in connection with their general practice. It nets the doctors a sizable extra revenue, as well as contributing a great deal to the welfare and health of literally millions of American families.

About eight miles northeast of Goshen, Indiana, and several miles' southwest of Middlebury, the doctors have set up their business. From U. S. highway No. 20, it looks like several ordinary quonset huts, but inside these four huts are housed 164 mares, from which are collected pregnant mare's urine for the preparation of the female hormones which are proving so valuable in medicine and in medical research. They lease the mares from neighboring farmers, test them for pregnancy, and then keep the pregnant mares in the huts throughout the winter. The hormone is extracted in a purified form at the Parke-Davis and Company laboratories in Detroit, to which the urine is shipped in 50-gallon drums.

The mares are bred by the farmers in June and come into the huts in October or November when the farm crops, including corn, are garnered. Then, when their usefulness in hormone production is at an end, they are released to the farmers, in time for spring ploughing. The percentage of hormone in the urine builds up starting at the 135th day of pregnancy, and reaches the peak about the 255th day.

The farmers are benefitted by having their horses well fed and cared for during the slack winter months, and humanity is served by the health-giving hormones conserved. The doctors, both graduates of Michigan State College, say the horses are fed the best of oats, mixed hay and alfalfa, in fact, when they are released they look better than they ever did before.

The quonset huts were set up in September of 1946 on Dr. Corson's 160-acre farm, where a lot of the feed, that is used, is raised. They picked this spot in the center of a community that is noted for its use of horse power, and promised the farmers if they would cooperate in leasing their horses for this purpose, that they would limit their leasing to this community. Since, they have turned down offers of hundreds of horses from other sources in order to keep that promise. Doctor House said that they have had about 50% repeats.

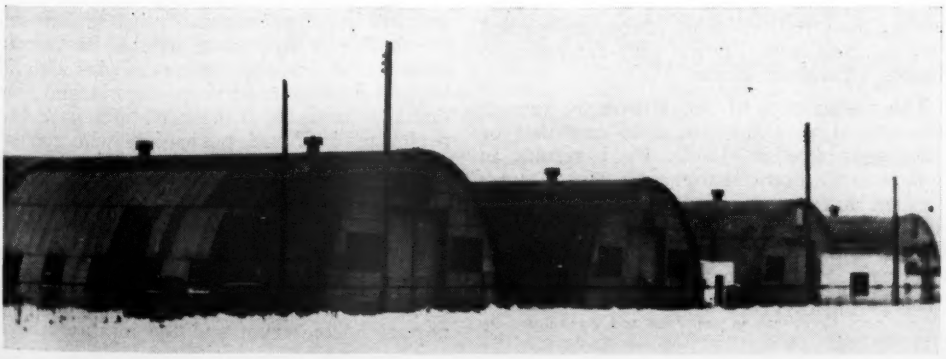
A barn manager and twelve other employees are required to operate the plant day and night. The mares are given the proper amount of exercise daily in a lot back of the plant. In connection with the barns there is also a sanitary—shall we say urine house—in any case it is on the order of a milk house in construction and equipment,

The doctors maintain a laboratory in Middlebury, in connection with their veterinary hospital, where pregnancy tests of the mares are made. To the end of 1947 more than 400 mares, that the owners thought pregnant, have been tested, but less than 50% have reacted positively. As another sideline, they have also purchased a registered champion jack for breeding purposes.

Since initiating this project they have taken in a junior partner, Dr. Alvin Dufour, also a Michigan State man, because each of the original partners now spends half of his time supervising and overseeing their side lines, *i. e.,* hormone production and standing the jack.

The original investment in this hormone enterprise was approximately $50,000. The partners are now pretty well out of debt. Of course the overhead is extremely high, as it includes wages for the foreman and twelve other employees, feed for the horses and many miscellaneous items.

According to Doctors Corson and House, the horses, which are rapidly decreasing in number, are at the same time becoming more necessary to medical science. They are vitally interested in seeing farmers breed more and better horses—Louise Purvis, Goshen, Ind.



Production and Use of New Biological Products Against Swine Erysipelas in Poland

By MARTIN M. KAPLAN, A.B., V.M.D., M.P.H.*

SWINE erysipelas is a historical enemy of the swine industry in Central Europe. Its economic importance surpasses that of hog cholera in most countries in this region. In Poland the disease is mostly encountered in its acute, fatal form. This virulence is attributed to the heavy contamination of the soil throughout the country as a result of continual seeding from the yearly epizootics that are encountered here.

The simultaneous inoculation of virulent culture and swine erysipelas antiserum has been the method most used in Poland to control the disease. In the simultaneous method used here, the serum and culture inoculation is usually followed in one to two weeks by a second inoculation of culture alone. In some districts where the second inoculation of culture alone is not performed, the simultaneous inoculation procedure is repeated four to six months later (spring and autumn). The simultaneous method is used in pigs after they are weaned. Immunity is achieved for a period of four to five months.

It was recognized that the simultaneous method, although giving temporary relief in stopping overwhelming losses, tended to perpetuate the disease because of the continual introduction of virulent organisms into the terrain. Thus, Polish veterinary authorities have been keenly interested in any possibility which would exclude the necessity of using virulent culture in the field for effective biological prophylaxis against swine erysipelas. The use of serum alone has the serious disadvantage of transient protection, and until recently little success has been experienced with killed or attenuated vaccines against swine erysipelas. It was with great interest, therefore, that claims of excellent results were received in Poland from the Soviet Union concerning the effectiveness of Muromcev's killed vaccine, and from France with reference to Staub's attenuated vaccine.

The preparation of the Muromcev vaccine was started in Poland in 1945 and that of Staub's vaccine in 1947. Field results in Poland with both Muromcev's and Staub's vaccines have been encouraging, but Staub's vaccine was felt to be the more practicable. These results have influenced the official Polish veterinary services to alter, drastically, their swine erysipelas prevention program for 1948. For the coming season Staub's vaccine and swine erysipelas antiserum will be the primary weapons used in Poland against swine erysipelas, and Muromcev's vaccine will be used only on a limited scale. If Staub's vaccine proves to be effective in an ambitious inoculation program scheduled for this spring, government authorities hope to eradicate swine erysipelas within a few years (an unlikely accomplishment in view of the heavy contamination of the soil). It is noteworthy, however, that large stocks of antiserum are being produced and held in reserve in the event of the failure of Staub's vaccine.

The methods of preparation of Muromcev's and Staub's vaccines as produced at the National Veterinary Production Laboratories (P. I.W.) in Poland, will be discussed in this paper. There will be described also, what appears to be, an interesting innovation in the hyperimmunization of horses for the production of swine erysipelas antiserum. It will be noted that many of the steps given in the various procedures are rather crudely performed because of the serious lack of adequate laboratory equipment and supplies. Refinements in technic here will have to await amelioration of the difficult working conditions, which at present beset the laboratories.

The writer has witnessed, but has not performed the production technics to be described, and he is merely reporting the procedures and claims of efficacy given by Polish veterinarians.

Staub's Vaccine

According to Trawinski[1] an attenuated vaccine against swine erysipelas was introduced in 1940 in France and French colonies in North Africa by Staub, of the Pasteur Institute. The first experiments in pigs with this vaccine were conducted in Algeria and since that time over 360,000 inoculations have been performed in French possessions with good results. The vaccine is avirulent for laboratory animals (white mice, pigeons) and pigs. The attenuated feature of the organism has remained constant to date.

The preparation and use of the vaccine according to Staub's instructions is as follows:[1,2]

One ml of formalin is added to 600ml of normal horse serum and the mixture shaken

*Veterinary Consultant in the Food and Agriculture Organization of the United Nations.

for 15 minutes. One ml of ammonium hydroxide is then added to neutralize the excess formalin. The mixture is thoroughly shaken and finally added to 1200ml of sterile distilled water. Forty ml of the diluted mixture is added to each liter of infusion broth containing 20 grams of peptone (Martin's) and five grams of sodium chloride, the broth being then adjusted to pH 7.5 and sterilized.

The media is seeded with Staub's attenuated strain of *Erysipelothrix rhusiopathiae* (a passage of which has been made every four days) and incubated for 48 hours at 35-37°C. Cultural tests for bacteriological purity are made and potency tests are carried out in mice. One-eighth ml of the vaccine immunizes white mice after 10 days to 1000 M.L.D. of 24-hour virulent culture of the erysipelas organism.

The vaccine must be used in the field as soon as possible after its preparation. Viability is given as one month under ordinary field conditions. Inoculations consist of 0.5ml subcutaneously regardless of age or liveweight of the pigs. Immunity develops after a period of 14 days and lasts approximately 8 to 12 months. It is advised not to use the vaccine during the hot months of the summer. Spring and autumn are the preferred seasons for inoculations. Furthermore, the use of the vaccine is contra-indicated in the face of an outbreak because of a negative phase of immunity which is supposed to occur during a two-week period following inoculation. Suckling pigs are inoculated in the vaccination campaign, although the resultant immunity is less strong and more transient than that achieved in pigs over three months of age.

Modifications in Staub's original instructions have been made in Poland. The step utilizing the mixture of normal horse serum and formalin in the preparation of the media is omitted and the broth media is adjusted to pH 7.8 instead of 7.5. No vaccine will be used in the field if it is over 10 days old from the date of preparation. This precaution will be taken this spring because field experiments performed in Poland last year revealed that vaccine, three to four weeks old, gave poor results. It is felt here that immunity is obtained for a period of only four months, in distinction to the 8 to 12 months duration given by Staub. Polish workers hope to augment the immunity by increasing the dose of vaccine for pigs weighing over 40 kilograms to 1ml instead of the 0.5ml originally advised by Staub for all sizes and ages of swine.

One group of laboratory workers in Poland observed sporadic deaths in mice from erysipelas septicemia within a few days following inoculation of 0.15 ml of Staub's vaccine. These losses have been very few considering the large number of mice which have been used experimentally, and the workers feel that Staub's strain of the erysipelas organism possesses little or no virulence for these animals. It has been found that between 70 and 80% of mice inoculated with 0.15ml of the vaccine will resist 1,000 M.L.D. of virulent *Erysipelothrix rhusiopathiae* culture when challenged 12 days after inoculation with the vaccine. Another group of researchers conducted experiments in which 60 mice were given graduated amounts of the vaccine and a different challenging dose of virulent organisms. The challenge dose used was 0.001ml of virulent 48-hour culture of *Erysipelothrix rhusiopathiae* which killed control mice in three days. One, 0.5, and 0.25ml inoculums of Staub's vaccine were used followed by a mortality of 10, 20 and 40% respectively to the challenge dose when it was given two weeks later. Limited trials made on five pigeons indicated that 0.5ml of Staub's vaccine given intramuscularly was not pathogenic in these birds, but the pigeons succumbed to a challenge dose of 0.2ml of virulent culture which was given 12 days later.

During the summer of 1947 the Polish veterinary services performed inoculations with Staub's vaccine in 19,990 pigs located in the Lublin, Wroclaw, and Poznan districts. Approximately 2.64% (528 pigs) were subsequently affected with swine erysipelas but the majority of these cases occurred within the first 14 days following inoculation of vaccine. Only 10 pigs were reported to have acquired swine erysipelas between the 14th day and 4th month after vaccination. Incomplete observations made by field veterinarians indicate that immunity waned four months following vaccination. Unfortunately, uninoculated control pigs were not allowed to remain in the same districts where vaccinations were performed so that no basic comparison can be made with inoculated animals concerning the incidence of disease. The incidence of disease in vaccinated animals, however, was far smaller than in previous years in these same districts. (It should be noted that the basis of reporting was clinical and not laboratory diagnosis.) The large inoculation trials conducted in 1947 were performed during the unfavorable summer season, and the Polish veterinary services were well impressed with the results and practicability of the vaccine.

A widespread inoculation program utilizing Staub's vaccine, and involving approximately four million pigs, has been planned for the spring of 1948. Seven laboratories located in different parts of the country will produce the vaccine. Inoculations will be performed only

during the months of March to May inclusive. Government veterinarians will place their order at the nearest laboratory for the necessary amount of vaccine no more than 12 days before actual use of the product. Preparation of the requested amount of vaccine in the regional laboratories will require two days and the vaccine will be used within the succeeding 10 days. Staub's vaccine will be used only in pigs over three months of age, and pigs under 40 kilograms in weight, will receive 0.5ml while pigs over 40 kilograms will receive 1ml of the vaccine. Swine erysipelas antiserum will be used at the time of weaning (eight weeks of age), and during the suckling period only if swine erysipelas threatens a district. As mentioned previously, large stores of antiserum will be kept at hand in the event of wholesale failure of the Staub vaccine.

Muromcev's Vaccine

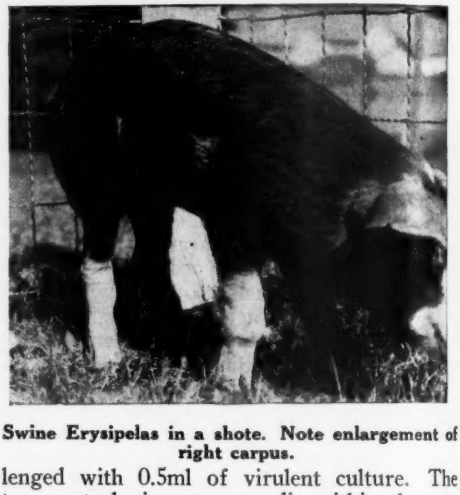
Preparation of the vaccine according to Muromcev's instructions is as follows:

Two liters of cold distilled water per kilogram of ground beef meat (horse meat is used in Poland) are mixed and allowed to stand for 12 hours, after which the mixture is boiled for 20 minutes and filtered through course filter paper or cotton. The filtered liquid is mixed with fresh beef liver cut into small pieces, 300 grams of liver being used for each liter of filtrate. The mixture is boiled for 30 minutes, filtered, and distilled water added to restore it to the original volume. One per cent peptone, 0.5% dibasic sodium phosphate, and 0.25% agar is then added, and the pH adjusted to 7.8. (It has sometimes been found necessary to decrease the amount of agar if the vaccine is too thick for convenient use in the field). The mixture is again boiled for 20 minutes, filtered, and 600ml quantities are poured into liter flasks. After final autoclaving the pH of the media should be 7.2 to 7.4.

The media should be prepared fresh for each batch of vaccine, and seeding of the organism must be made no later than five days after preparation of the media. The seed culture should be prepared from virulent strains of *Erysipelothrix rhusiopathiae* which have been recently passed through pigeons.

The seeded flasks are incubated at 34 to 35° C for six days. During the first three days of incubation the media becomes cloudy, but it becomes clearer during the ensuing three days. At the end of the inocubation period smears are made, and agar plates are introduced to determine the purity of culture. Sufficient formalin (containing approximately 40% formaldehyde) is added to the cultures to make a final concentration of 0.3% and the flasks are incubated again for 48 hours at 34 to 36°C. The final pH of the now finished vaccine is adjusted to 7.0 to 7.2.

Cultural tests are made for sterility, and the establishment of nonvirulence and antigenicity are determined by the inoculation of pigeons. Three pigeons are used for this purpose. One pigeon receives 3ml of the vaccine, and two others 1ml each. Three weeks later the three inoculated pigeons plus two controls are challenged with 0.5ml of virulent culture. The two control pigeons must die within three to four days, and the death of one of the pigeons which had received 1ml of vaccine is permissible for a batch of vaccine to be issued for field use. Approximately 40% of the vaccine produced fails to pass the potency test and is discarded or mixed with a new batch of vaccine and retested.



Swine Erysipelas in a shote. Note enlargement of right carpus.

The potency of the Muromcev vaccine is valid for at least 10 months after its preparation, and the immunity achieved by inoculated pigs was stated to have a duration of approximately five months. Inoculations (intramuscular) of 5ml of the vaccine are performed twice at 7 to 10 days interval in animals over five months of age and a total of three times in younger animals with the third inoculation acting as a booster after the animal reaches five months of age. The peak of immunity is not reached until 15 days after the last inoculation.

Muromcev and Matviyenko[5], in 1934 studied the behavior of different groups of microorganisms in liquid media containing 0.25 to 0.50% agar. They felt that the changes in density, surface tension, and osmotic pressure brought about by the addition of agar created an environment for the microorganisms analogous to that found in the animal body. For example, in this "agaro-bouillon" anthrax bacilli produced capsules but sporulation was checked, which is similar to what occurs *in*

vivo. Also when grown in this media, the hemorrhagic septicemia group of organisms showed prominent bipolar characteristics, and *Erysipelothrix rhusiopathiae* were uniform and thin in appearance, morphologically resembling those species of microorganisms as found in infected animals. Furthermore, the swine erysipelas organism grew luxuriantly in this media so that the production of a vaccine was felt to be feasible.

After encouraging preliminary experiments with the Muromcev vaccine were carried out in pigeons and pigs in 1934 and 1935, large scale inoculations in swine were performed in the Soviet Union between 1936 and 1938.[5,6,7] Over one million pigs were inoculated. Approximately 0.32% of the pigs subsequently were affected with swine erysipelas in a six-month period following vaccination. None of the illnesses or deaths were attributable to any harmful effect of the vaccine itself, because the majority of losses occurred more than 14 days following the last inoculation of the vaccine. Unfortunately, the original Russian literature was unavailable and no details could be obtained concerning the morbidity rate in inoculated pigs in the same districts. It is therefore difficult to evaluate, accurately, the efficacy of the vaccine in this group of inoculations. During the occupation of Poland and the Ukraine, the Germans experimented with the Muromcev vaccine but the results of their work is not known to Polish authorities.

In the Lwow district in 1940-41, Podgorski inoculated over two thousand pigs with the Muromcev vaccine.[8] He reports that excellent protection was conferred on inoculated pigs but that immunity lasted only four to five months.

In 1945-46 Majdan[9] carried on some limited experiments to determine the value of Muromcev's vaccine in pigs under Polish conditions. Twenty pigs were used in a laboratory experiment, and 192 pigs were inoculated in a district where swine erysipelas was enzootic. In the laboratory experiment, 13 pigs received two 5ml inoculations of the vaccine given two weeks apart, one pig received one inoculation of 10 ml of the vaccine, and six pigs were used for controls. Groups from these 14 pigs were tested every month for six months after inoculation by scarifying the skin and rubbing virulent *Erysipelothrix rhusiopathiae* into the wound. Resistance was gauged by the lack of reaction (fever, local erythema, malaise). Only small reactions were obtained in a few of the vaccinated pigs, whereas of the six controls one died of artificial infection, one died from natural infection of erysipelas contracted during the course of the experiment, three showed marked reactions, and one showed no reaction.

In the field experiment, two of the 192 vaccinated pigs contracted clinical swine erysipelas but they recovered after receiving swine erysipelas antiserum. Unvaccinated pigs in the same herds contracted swine erysipelas. The number of unvaccinated pigs affected could not be obtained from the peasants because no indemnity was paid as was done in the case of vaccinated pigs. Sows vaccinated late in pregnancy showed no ill effects from the vaccine.

A large field experiment involving 17,410 pigs was conducted by veterinarians in the Warsaw district in 1946, during the height of the swine erysipelas season.[10] Two inoculations of 5ml of vaccine given one to two weeks apart were performed, except in one group of 300 pigs in which three inoculations were given. A morbidity of 0.75% (127 pigs) of clinically diagnosed swine erysipelas occurred within 14

Skin form of swine erysipelas.

days after the last inoculation. This morbidity was attributed to the lack of time after vaccination for the adequate development of immunity. Between 14 days and four months after the last inoculation of the vaccine 0.33% (58) of the inoculated pigs sickened with the disease, mostly in its benign form. In one of the districts an opportunity was afforded to compare the morbidity in 2162 swine inoculated by the simultaneous method (serum and culture) and those inoculated with the Muromcev vaccine. In the period up to 14 days following

serum and culture inoculation 0.2% (six pigs) sickened with swine erysipelas. From the 14th day to the 4th month following inoculations and additional 0.1% (three pigs) fell ill.

It is apparent that great difficulty arises in attempting to evaluate the collected data given above because of the lack of control groups of uninoculated animals within the same herd or even in the same district. Furthermore, statistics covering swine in Poland are usually undependable because of the traditional reticence of the peasantry where reportable animal diseases are concerned. Field veterinarians are divided in their opinions concerning the practicability of the Muromcev vaccine, but nearly all of them agree that the vaccine gives good protection for a period of about four months. The main objections to the use of the Muromcev vaccine are the necessity for at least two inoculations (deeply intramuscular), and the lag of two to three weeks after the last inoculation before the development of immunity.

The Hyperimmunization of Horses for Serum

A new procedure was inaugurated in the veterinary laboratories in Pulawy in 1946 in an attempt to offset the great losses from bacterial endocarditis and arthritis in horses subjected to the usual hyperimmunizing procedure for the production of swine erysipelas antiserum. The important principle in the new procedure is the subcutaneous inoculation of a concentration of agglutinated swine erysipelas organisms instead of the usual intravenous inoculation of large amounts of whole culture. Trawinski,[11] Director of the National Veterinary Production Laboratories in Poland (P.I.W.), states that he began to use this method in 1932, and since that time over 250 horses and 32 rabbits have been used in his experiments. Routine application of his procedure, however, was not begun until 1946 at the Pulawy branch of the P.I.W.

The antigen is prepared by seeding liter flasks containing horse meat infusion broth (peptone-free) with two loops of 24-hour old cultures of the erysipelas organism, and incubating the flasks for 24 to 36 hours at 37°C. (If large quantities of antigen are needed quickly, 5 to 10ml of culture are added to each flask and incubated four to six hours.) Ten ml of swine erysipelas antiserum having a titre of at least 100 units are added to each liter of culture, and the mixture is incubated for five to six hours at 42°C. When a flocculent precipitate becomes visible the flasks are placed in a refrigerator (8°C.) for a few hours or overnight until sedimentation occurs, after which the supernatant fluid is siphoned off. The yield of sediment from each liter of culture is approximately 10ml of agglutinated organisms.

Trawinski[11] asserts that the use of subcutaneous injections of agglutinated organisms in horses usually yield swine erysipelas antiserums containing titres of 200 to 300 units (see below for unit measurements). In his description, hyperimmunizations were begun with a subcutaneous inoculation of 5ml of agglutinated sediment. The inoculums were increased by 5ml quantities each time for seven further weekly inoculations, and at the end of the series titres of 150 to 200 units were obtained. A few more weekly inoculations of 40ml of agglutinated sediment often increased the potency to 300 units or more. Later work carried out at Pulawy on more horses, however, revealed that Trawinski's original results were exceptional. The usual potency titre now obtained is 100 to 150 units. Certain modifications have been introduced in the procedure originally given by Trawinski, and the method of hyperimmunization now used (February, 1948) in Poland follows:

A. Inoculate at 5-day intervals the following quantities of 24 to 36-hour-old, plain bouillon cultures of *Erysipelothrix rhusiopathiae:*

1. 10ml subcutaneously
2. 30ml subcutaneously
3. 50ml subcutaneously
4. 30ml subcutaneously, and 20ml intravenously
5. 50ml intravenously
6. 50ml intravenously

B. Start subcutaneous inoculations of agglutinated sediment.

7. Agglutinated sediment (approximately 2.5 ml) which represents the product of 250ml of culture.
8. Seven days later increase inoculum to agglutinated sediment (approximately 5ml) from 500ml of culture.
9. Repeat step No. 8 every seven days augmenting the inoculum each time by 2.5ml (representing 250ml of culture) until 20ml of inoculum is reached.
10. Repeat 20ml inoculums every seven days until titre of serum is satisfactory.
11. Bleed (about 1% of liveweight) 11 days after the last inoculation of agglutinated organisms. Perform a second bleeding five days later.
12. Five days after the second bleeding inoculate 15ml of agglutinated culture (representing yield from 1500ml of culture).
13. Repeat steps 11 and 12.

The subcutaneous inoculations of the agglutinated sediment are made along the course of the neck. In two to three days the horse is usually feverish and lacks appetite, but re-

covery occurs within one to two days. Large swellings often occur at the sites of inoculation but they usually subside within one week unless secondary contamination has caused the formation of an abscess. Only two of 15 horses used for this procedure showed arthritis and lameness in the course of nearly two years. Records at the Pulawy laboratory reveal that with the old culture method horses remained in effective production for approximately 15 to 18 months, and deaths or severe disability occurred in 20 to 25% of the horses yearly. Horses which show signs of breaking down from the intravenuous inoculation of culture are now transferred to subcutaneous inoculations of agglutinated sediment. This has been done in 20 horses and has effectively prolonged their usefulness.

Utilizing the complete course of hyperimmunization as outlined above, titres of serum containing 100 to 150 units are regularly attained. Unit measurements are patterned after a German method. The serum control test is performed as follows:

Twelve mice weighing approximately 15 grams each are divided into six groups of two mice:

	Survival Unit Score
Group 1 receives 0.005 ml serum subcutaneously	300
Group 2 receives 0.0075ml serum subcutaneously	200
Group 3 receives 0.01 ml serum subcutaneously	150
Group 4 receives 0.015 ml serum subcutaneously	100
Group 5 receives 0.02 ml serum subcutaneously	75
Group 6 controls	

One hour after inoculation of the serum all of the mice are injected intraperitoneally with 0.01ml of a 24-hour virulent culture of *Erysipelothrix rhusiopathiae*. The mice are observed for eight days and the control mice must die within that period. The unit score given to the serum depends upon its protective ability in the various groups of mice. Inconsistencies are encountered in this test which necessitate a repetition of the procedure. For example, Group 3 may survive whereas one or both mice in Group 4 may die. When larger numbers of mice were available the method described gave fairly clear-cut results, and repeated check tests were seldom necessary. Batches of serum having less than 100 units are mixed with more potent stock and retested. No serum is released into the field having less than 100 units. (It is interesting to note that serum sent to Poland from the United States by UNRRA in 1946 often revealed a titre of less than 100 units according to this test.)

Swine erysipelas antiserum obtained from hyperimmunized sheep is used in Poland for erysipeloid in human beings because serum from hyperimmune sheep causes less severe reactions than does horse serum.

Summary

The preparation, use, and limitations of Staub's and Muromcev's vaccines against swine erysipelas in Poland are discussed. Although experimental and field observations in over 40,000 pigs in Poland are incomplete, both vaccines appear to have good protective value. Their chief asset rests on the use of killed or attenuated organisms, as contained in Muromcev's and Staub's vaccines respectively, in order to achieve immunity. The immunity obtained, however, appears to be of relatively short duration (approximately four months). Staub's vaccine is more practicable in the field. A mass inoculation campaign utilizing Staub's vaccine will be carried out in Poland during 1948. This campaign should provide a definitive test of the efficacy of Staub's vaccine because of the severely enzootic-epizootic nature of swine erysipelas in Poland.

There is also described the use of agglutinated *Erysipelothrix rhusiopathiae* organisms, instead of whole culture formerly used, for the hyperimmunization of horses in the production of swine erysipelas antiserum. The advantages of this new method lie in the resultant diminished toxic reactions to inoculations of antigen, and the extended usefulness of horses subjected to the hyperimmunization procedure.

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Immunity Against Canine Hookworm Disease[1]

By G. F. OTTO'* Ph.D.
Baltimore, Maryland

THE layman's concept that some children and animals are "just naturally wormier than others" has not been wholly dispelled. Indeed, while this statement apparently disregards a whole array of scientific data, it is nevertheless a reasonably good summary of the actual situation which develops from the interreactions of the various dynamic forces which are operative in the epidemiology of an infectious disease. Some dogs and children live under conditions which "just naturally" predispose to infection.

The staff and graduate students in this department, for nearly three decades have carried on field and laboratory studies designed to give us a better understanding of the interreaction of some of these factors in the epidemiology and control of hookworm disease in man. Most of these studies have had the direct financial support and cooperation of the staff of the International Health Division of the Rockefeller Foundation. Laboratory studies have been carried out with the dog hookworm, *Ancylostoma caninum,* in its normal host as well as with other parasites in other laboratory hosts so that the results should be of direct interest to the practicing veterinarian. These studies have led us to the following conclusions:

1. Sublethal infections with hookworm are capable of stimulating and do stimulate a powerful and highly protective immunity to hookworm *disease;* immunity develops much more rapidly in mature animals than in puppies or growing animals.

2. A few hookworms are of themselves of no serious concern in the health of the dog and many lead the owner or veterinarian to overlook some more fundamental cause of debilitation and illness.

3. Serious acute hookworm disease develops only under conditions which permit the acquisition of large numbers of infective hookworm larvae either as a single initial infection or as rapidly repeated or continuous infection early in the exposure. Such exposure is the type seen in young puppies under crowded conditions or poor sanitation.

4. Debilitation from dietary deficiencies, and perhaps from concurrent disease as well, directly or indirectly, disrupts the normal immunological responses and leads to chronic hookworm disease with chronic anemia and further debilitation. Thus chronic hookworm disease develops in young or old dogs where there is repeated or continuous exposure to heavy infection while the animal is debilitated by concurrent dietary deficiency. It is more important to correct the diet and improve the sanitation than to remove the infection by therapy.

It must be recognized that the above generalizations are subject to wide variation under different local conditions, but I believe that they cover the basic principles involved. An attempt will be made here to summarize the field and laboratory studies which have forced us to these conclusions. The earliest experimental studies in canine hookworm infections in this laboratory suggested that puppies were less refractory than mature animals and offered some evidence that upon repeated infection animals became progressively more resistant. However, many of these experiments utilized street dogs of unknown age and uncertain infection history and were accordingly very difficult to interpret. It is important to note for a full appreciation of experiments of the type reported here that we did not obtain consistently repeatable results until we utilized only animals either reared in the laboratory or obtained during the suckling period or at weaning time; the latter were purchased from homes in the congested part of the city. It is equally important to note in connection with these experiments that, while nearly every puppy purchased at weaning time harbored ascarids (*Toxocara canis*), which were removed with tetrachlorethylene or hexylresorcinol, not a single one was ever found to be infected with any hookworm. Each given experiment was set up with a group of litter mate animals divided in such a manner that at least one litter mate was maintained as "control" on the experimental procedure.

Development of a Protective Immunity

Using this type of approach, McCoy (1931) first clearly demonstrated that animals receiving infective larvae of *A. caninum* in small doses over a period of months became increasingly refractory to infection. When the larvae were administered too rapidly the animals usually developed acute hookworm anemia but if they survived the acute attack they were thereafter refractory to attempts at reinfection.

1 Invited paper, presented at the 18th annual meeting of the Florida Veterinary Medical Association, St. Augustine, Oct. 27 and 28, 1947.

*From the Department of Parasitology, School of Hygiene and Public Health of the Johns Hopkins University, Baltimore, Maryland.

However, the previously uninfected litter mates were often fairly resistant to infection at the end of the experiment and questions were raised as to whether or not the increasing age of the animals was not in part, if not primarily, responsible for this increasing resistance. Accordingly a series of experiments were designed (Otto & Kerr, 1939) to develop hyperimmune animals, if possible and challenge that immunity with infections which would be fatal to the non-immunized litter mates. Thus, the animals to be immunized were given initial subcutaneous injections of 15 infective hookworm larvae and thereafter at intervals of approximately four days were given increasing numbers of larvae until five to seven months later they had received a total of 120,000 to 240,000 larvae in this manner without ever showing any physical signs of hookworm disease. Furthermore, as judged by the daily hookworm egg outputs there was no period at which any appreciable numbers of hookworms had become established. Accordingly, these dogs and their previously uninfected litter mates were given identical heavy subcutaneous doses of infective larvae (120,000 to 200,000 in the different experiments). In no case was there any evidence that worms from this challenging infection became established in these immunized dogs; post-mortem examination revealed only the relatively few mature worms from the earlier immunizing infections (Litters B, E, F, table I). On the other hand the three non-immunized, i. e. previously uninfected, animals in Litters E and F (table I) died from acute blood loss, i. e. acute hookworm anemia, within two weeks and on post-mortem examination harbored 11,000 to 31,000 immature hookworms from the challenging infection. In the third litter in this series (Litter B, table I) due to unavoidable difficulties the challenging dose contained many immature larvae and resulting infection was not fatal to the non-immunized dog although over 1200 worms developed. This was the only non-immunized dog in our entire series which survived infections of this general magnitude. Thus these experiments seem to clearly demonstrate that graded infections given slowly over a long enough period to avoid severe blood loss are capable of producing a highly protective immunity.

Table I.—Showing the Number of Hookworms Recovered from Immunized Dogs and Their Non-immunized Litter Mates After Test Infections Fatal, in All But One Case, to the Latter

Litter	Immunization Period (days)	Age at Test Infection (days)	No. Larvae in Test Infection	Worms Recovered from Litter-mates Immunized	Non-immunized
A	350	457	200,000	80	12,200
B	215	323	200,000*	52	1,263*
				56	
C	210	360	129,000	371	54,370
D	188	351	200,000	5	3,208
E	160	229	120,000	118	13,550
				203	
F	147	281	178,000	75	11,370
				136	31,170
G	138	376	1,031,000	2,519	48,700
H	85	332	200,000	260T	58,940
				985	
I	50	179	200,000	220T	68,070
				811	
				1163	
				1347T	

*Some larvae in test infection were not fully developed to infectious stage; non-immunized animal did not die.
T=Treated throughout the period of immunization to prevent the maturation of the worms from the immunizing infections.

Accordingly experiments were designed (Otto, 1941) to determine whether or not similar infections by mouth would also be effective in producing a protective immunity, to determine something of the degree of immunity which could be induced by severe infections, and to ascertain whether or not immunity could be induced by larval stages without the maturation of the adult worms.

Particular attention was given to the question of possible immunization resulting from *per os* infections because this appears to be the common route of infection under natural conditions and since there is essentially no migration out of the alimentary canal follow-

ing initial *per os* infection (Foster and Cross, 1934), in contrast to the extensive migration through various tissues following percutaneous or subcutaneous infection. Accordingly litters A. C. and D (table I) were handled in essentially the same manner as those already discussed except that all infections, both the immunizing and challenging infections, were administered *per os* in hard gelatine capsules to insure against infection through the lips or buccal mucosa. Again the series of graded infections rendered the animals immune, no worms establishing from the challenging infection, whereas the non-immune, i. e. previously uninfected, litter mates were, without exception, killed by this infection.

The two animals in Litter G (table I) may be cited as evidence that the immunity is not an absolute, but rather a relative, condition. The immunizing larvae were administered over a shorter period of time and the challenging dose was raised to a million larvae. The immunized animal in this litter is the first in our series which developed anemia during the process of immunization comparable to some of those in McCoy's experiment but like McCoy's animals it had entirely recovered and was refractory to the later immunizing infections before the administration of the challenging infection. Nevertheless when this animal was killed 16 days later, after the non-immunized animal had died, it was found to harbor 2519 worms. Of these 2478 were immature worms apparently from the challenging infection and only 41 were mature worms from the immunizing infections. While this animal was not as completely immune to over a million larvae as the immunized animals in the previous litters had been to 120,000 to 240,000 it was nevertheless much more refractory than was its previously uninfected litter mate. Furthermore it suffered only a slight blood loss from the over 2500 worms whereas scarcely more worms killed the non-immunized animal in litter D.

The last two litters in this series (litters H and I, table I) were used to shed more light on the question of possible immunization by giving the immunizating infections over a much shorter period and at the same time prevent in part of the animals the anticipated blood loss during this period by removing the developing worms before maturation. In both litters the animals to be immunized received the immunizing infections subcutaneously within a much shorter time (50 and 85 days) than in the previous experiments, and one-half of them were given tetrachlorethylene weekly throughout the period of immunization. The untreated animals were still very anemic when the challenging infection was administered whereas those receiving weekly treatments of tetrachlorethylene, and thus spared the blood sucking attack of the adult worms, were essentially normal throughout. However the latter were no more immune than the former, both groups being less immune than the previously immunized animals challenged with 200,000 larvae. It would appear that a significant immunity can be operative despite the acute anemia in these animals and that an equally effective immunity can be stimulated by the larval stages alone, i. e. without the development of the adult worms. The non-immunized animals again died in both these litters. It is probable that the period of exposure is of more than casual importance in producing the maximum degree of immunity. Thus the 50 and 85 days of exposure to the immunizing infections in these last two litters may not have been sufficient to produce the complete protection obtained in litters A to F.

Nevertheless, it is evident in the above series of experiments that regardless of certain variations in the manner and time of administering the initial infections, sufficient immunity develops in animals serially infected to protect them from an otherwise lethal infection.

Quantitative Aspects of Immunity

It has already been noted that the immunity which develops is not absolute but a quantitative phenomenon. Specifically it has been suggested that the time of exposure to the hookworm may have an important bearing on the intensity of the resulting immunity. Likewise it will be recalled that exposure, in graded doses, to a total of 120,000 to 240,000 over a period of five to ten months renders an animal completely refractory to a challenging dose of up to 200,000 larvae. On the other hand the one such animal which received a challenging dose of a million larvae was only partially immune to such a dose. Time has not permitted an exhaustive study of the many possibilities of such quantitative relationship. However, preliminary experiments were carried out which demonstrate more clearly that there are such quantitative relationships. An initial infection of 1200-1400 larvae were shown, subsequently, to protect dogs from otherwise lethal infections whereas an initial infection of only 300 larvae did not provide such protection.

In these experiments one-half of a litter was given a single sub-lethal, immunizing infection, subcutaneously, and two to four months later a challenging dose of 50,000 larvae was given to the entire litter (Otto, 1941a). In two such litters the animals to be

immunized received 1,200 and 1,400 larvae as the immunizing infection. These infections produced a critical but non-fatal anemia. Nearly two months were required for these dogs to throw off the worms, recover from the anemia, and be otherwise restored to good health. When challenged thereafter with 50,000 larvae these animals were almost completely refractory, harboring when killed only 109 to 330 worms. This type of experiment was repeated with two more litters but only 300 larvae were given as the initial or immunizing infection. This infection was not heavy enough to produce any demonstrable anemia and when the challenging infection of 50,000 larvae was given, there was very little evidence of immunity since three of the five animals died and were found on necropsy to harbor 3,000 to 10,000 worms; even the two which survived to the 15th day and were killed then harbored 2,200 and 6,900 worms respectively. Six of the seven litter mates, in these two sets of experiments, which received only the challenging infection of 50,000 died and harbored from 6,000 to 30,000 worms; the one which survived to the 15th day harbored, when killed, 4,600 worms. Subsequent experiments have offered the suggestion that while an initial infection of 300 larvae will not protect against the lethal effects of 50,000 larvae it may protect against 10,000 larvae. Thus it seems evident the immunity is not absolute but is a quantitative phenomenon which may be viewed as part of a fluctuating dynamic equilibrium.

The Demonstration of a Circulating Antibody

An attempt was made, by use of the methods of passive transfer, to determine whether or not this highly protective immunity involved a circulating antibody. In the first of these experiments nearly 200cc of serum from a hyperimmunized dog was injected into each of two puppies in a litter at the time they were infected with 5,200 larvae; the serum was divided into three doses and administered the day before infection, the day of infection, and the day after. Some partial degree of protection was afforded as compared to the fatal results in the untrialed puppies but the experiment was not conclusive. Accordingly, another approach was used with the second experiment involving 13 puppies of two litters. Five of the puppies each received subcutaneously 500 larvae which had been incubated at 37.5°C. for 1 to 3½ hours in serum from a dog which had been hyperimmunized.* The puppies were killed 16 days after infection and harbored on the average only 79 worms. In contrast to this the four litter mates which received 500 larvae similarly incubated in normal serum and the four which received 500 incubated in physiological saline, harbored respectively averages of 244 and 282. Thus over three times as many worms developed from larvae incubated in saline or normal serum as developed from those bathed in immune serum (Otto, 1940, 1940a)

A microscopic study of the larvae incubated in the immune serum for 3½ hours failed to reveal any change in appearance or activity. However, after five hours incubation fine granular or bubble-like precipitates appeared at the oral opening similar to that reported by Sarles (1938) for *Nippostrongylus muris* larvae; at this time the larvae were hyperactive, appearing almost as though they were trying to dislodge the adherent material. Thereafter the precipitate increased in amount, in some cases it appeared at the excretory pore as well, and in a few cases at the anal opening (plate I). At the same time the larvae became progressively less active; many were sluggish within 24 hours and most of them were very quiescent after 48 hours; some died as early as 48 hours and many were dead by the fifth or sixth day. In the meantime larvae in normal serum showed no signs of such precipitates and were active for periods up to two weeks; an occasional larva in the normal serum actually developed and went through an ecdysis into the next stage.

Thus it is evident that the serum of an immunized dog contains a substance which is toxic for the larvae; forming a visible precipitate within five hours and producing in less than 2½ hours a deleterious effect upon their capacity to develop.

Tissue Reaction and Allergic Manifestations

Sarles (1929) reported an inflammatory response in the skin at the cite of infection in mature dogs, and Stumberg (1932) demonstrated that larvae were retained and destroyed in the inflammatory reaction. Neither author, however, associated this reaction with the development of immunity since this phenomenon had not yet been clearly demonstrated. Kerr (1936), however demonstrated in experimental infections in mice that the hookworm larvae of the initial infection moved through the skin of mice and subsequently made their way with equal facility through the lungs to reach the intestine via the trachea and esophagus. On the other hand in mice rendered immune by repeated infections, the larvae were trapped in an intensified inflammatory reaction in the

*Hyperimmunized by repeated injection of large numbers of infective larvae after it had been shown to be immune to 100,000 larvae.

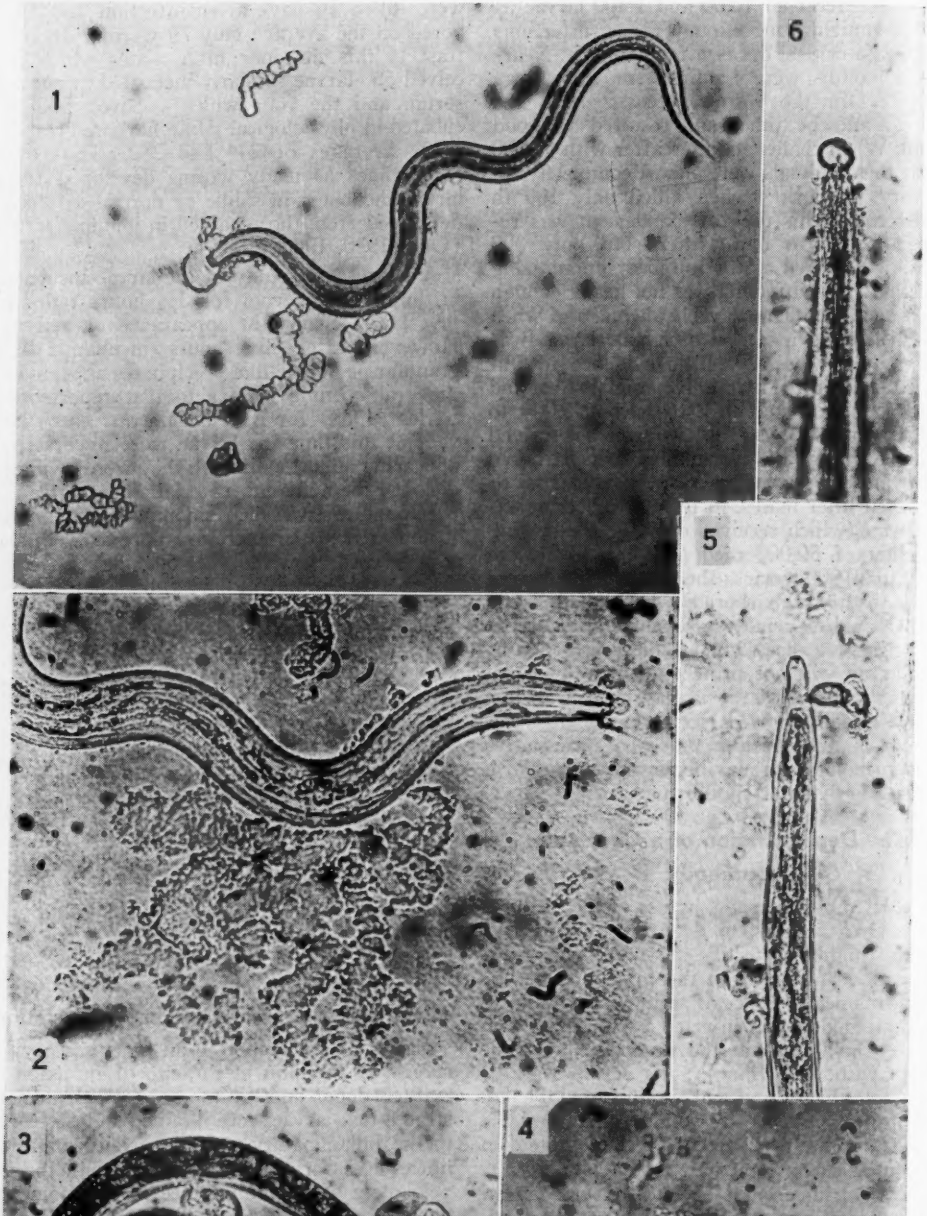
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PLATE I. PHOTO-MICROGRAPHS OF INFECTIVE LARVAE OF THE DOG HOOKWORM IN IMMUNE SERUM.

Figure 1. Precipitate at oral and excretory openings, smaller amounts attached to cuticula of larva, and larger masses broken free of the larva—48 hours.

Figure 2. Enlargement of reaction similar to that above; small bubbles at oral opening and along cuticula, large mass at excretory pore—48 hours.

Figure 3. Bubble-like precipitates at oral and excretory openings—24 hours.

Figure 4. Mass of granular precipitate completely enveloping the oral end of the larva—48 hours.

Figure 5. Ensheated larva with precipitates extending through sheath both at the oral and excretory openings—24 hours.

Figure 6. Small ring-like precipitate at oral opening and cuticular swelling just back of oral opening—24 hours.

skin and comparatively few escaped to continue the migration. Similarly when infections were given *per os* an inflammatory response which engulfed the larvae developed in the stomach and intestine. The inflammatory response was similar to the usual foreign body reaction with the ultimate destruction of the larvae. It is interesting, and I think sufficient, that in the non-immune animals some cellular infiltration occurred in the skin along the course of the larval migration but that this cellular response was not intense and rarely occurred around the larvae in sufficient quantity to immobilize it. Apparently the inflammation did not catch up with migrating larvae in the non-immunized animals. It seems reasonable then to assume that in the immunized animals the larvae were partially or wholly immobilized by the serum just as they are *in vitro* and their capacity for progressive migration was reduced or prevented thus permitting their engulfment by the cellular elements in the resulting inflammatory response. This has been studied more extensively by Taliaferro and Sarles (1939, 1942) who have demonstrated the precipitate in the buccal cavity and esophagus of *Nippostrongylus muris* in the tissues of immunized rats. They note that, although the skin is the first and apparently most effective tissue in destroying the larvae in immunized animals, some larvae escape and may be destroyed in the lungs. Still others complete the migration to the intestine before being killed, and a few may actually become established and mature.

We have not made extensive studies of the histopathology of our immunized dogs but the gross picture is very illuminating. When the larvae are administered at close intervals three to seven days for long periods, even when the later doses of larvae may be very large, the resulting inflammatory response in the skin is evident but not extreme. However, with the dogs listed in table I, usually an interval of three to six weeks intervened between the last of the immunizing infections and the final challenging infection. Thus following the challenging infection, not only did a marked inflammatory condition develop but usually there was an extensive exfoliation comparable to that seen in Arthus phenomenon (plate II). Thus not only did the immunized animal protect itself by the cutaneous reaction, but there is evidence of a powerful and tissue destroying allergic reaction. This was never seen in the nonimmunized animals which received the same challenging infection. Thus it seems probable that sensitization occurred along with immunization but that when the larvae were administered at close intervals during the immunization period they maintained at the same time a partial desensitization.

Not only were the larvae apparently destroyed in the inflammation and perhaps to some degree removed by the exfoliation of the skin, but it seems likely that comparatively few larvae migrated beyond this organ in the immunized dogs since they were particularly scarce in the lungs. Although a few appeared to be destroyed in the lungs it seems likely from the gross appearance and from the work of Kerr (1936) and Taliaferro and Sarles (1939) that the lungs are not primarily concerned with the destruction or elimination of the larvae by the immunized animal. Nevertheless, following the challenging dose the immunized animals frequently suffered pulmonary edema. Moist rales could sometimes be heard by the third or fourth day, but usually cleared up in a few days and was never a serious condition. We interpret this as another aspect of the allergic reaction.

The alimentary canal also plays its part as an immunological barrier and when infection is *per os* it is the primary if not the exclusive site of the immunized host's attack on the new infection. Since hookworms administered *per os to* the normal host do not usually undergo any migration from the gut or even penetrate the gut wall there is usually no cellular infiltration. Apparently the worms are immobilized or otherwise intoxicated by the precipitin reaction as soon as they start sucking blood and are thereafter carried out by the normal or in some cases, intensified peristaltic action

NOTE.—The author is indebted to Evelyn Allen Lewert for making most of the photomicrographs and for helping with the remainder of the photographs and photomicrgraphs in plates I and II.

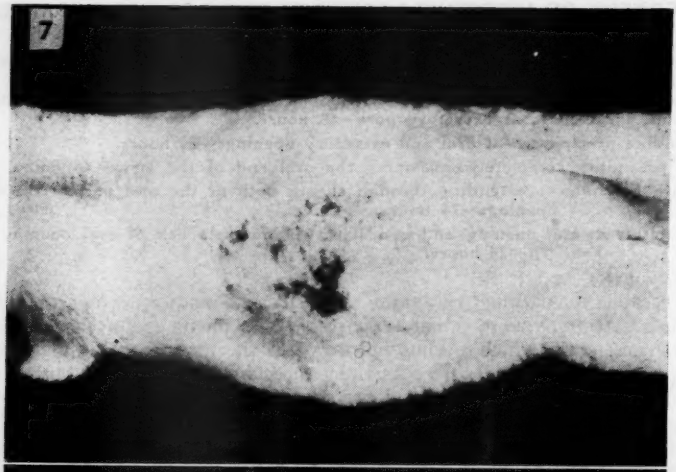

Figure 7. Reaction to 20,000 larvae on skin of non-immune puppy; frequently with initial infections of this magnitude there is even less reaction.

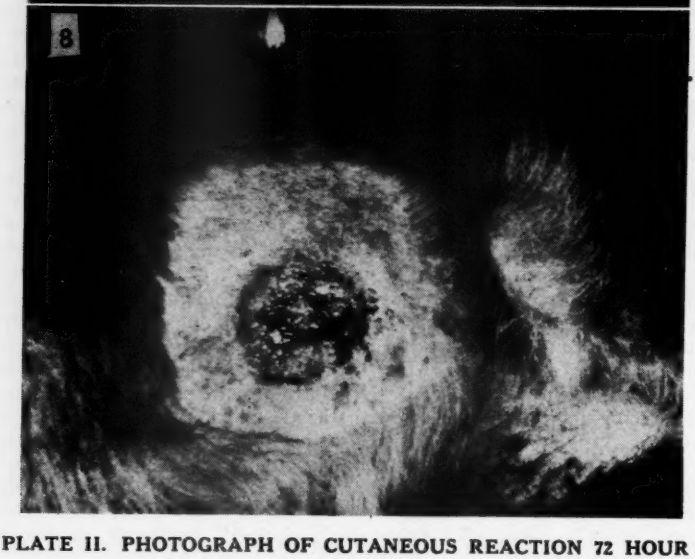

Figure 8. Reaction to 20,000 larvae on skin of hyper-immunized dog; this is typical of the reaction seen in such animals.

PLATE II. PHOTOGRAPH OF CUTANEOUS REACTION 72 HOUR AFTER INFECTION.

of the alimentary canal. Frequently the alimentary canal is edematous and hyperemic and a bloody diarrhea results for a few days. This again is apparently an allergic reaction since even with challenging doses of 200,000 there will be no evidence of traumatic injury or other evidence of blood sucking in the immunized dogs.

Malnutrition as a Predisposing Factor in Hookworm Disease

From the foregoing discussion and similar studies with other nematode infections in a variety of hosts one might easily draw the conclusion that chronic worm infection of disease producing levels is extremely rare, if indeed, it is not impossible. Obviously such a generalization would be in direct conflict with the well established evidence of chronic worm diseases in man and his domesticated animals. Perhaps the outstanding examples of such chronic debilitating worm infections are the hookworm diseases of man and dogs. It has been well established that chronic hookworm disease in man occurs in populations in which the nutritional status is far from optimum; usually there are obvious nutritional diseases present. Accordingly we have considered experimentally the role of nutrition in relation to hookworm disease in dogs.

In one series of experiments (Otto and Landsberg, 1940b) 13 puppies in two litters were all killed by initial infections of 900 hookworm larvae while on a grossly deficient

diet; the same dose of larvae either produced only a slight transient anemia or no ill-effects upon the litter mates receiving the normal stock diet. Deaths occurred with the animals on the deficient diet, as early as the sixth and as late as the forty-fifth day after infection. This is an extreme type of malnutrition since the diet was essentially devoid of all nutritional elements; such as protein, vitamins, and mineral salts; it consisted of cornstarch, 35%; uncooked dried peas, 35%; mazola oil, 29%, and sodium chloride (c.p.), 1%. It is estimated that this diet, which they ate freely, provided no more than 7.5mg of iron and less than 25mg of protein daily; furthermore, the peas, which were the sole source of protein, are deficient in some of the essential amino acids. Since iron salts are frequently used in the treatment of anemia 3,000 to 6,000mg of iron-ammonium citrate was given daily to half the dogs on this diet. The iron did result in a better regeneration of the red blood cells but it did not prevent or even delay the development of the fatal anemia. Thus dogs on a diet deficient in proteins and vitamins, with or without the addition of readily available iron, were bled to death by a single infection of worms (900) which had little or no effect upon their well nourished litter mates.

Of even greater significance, I think, is the demonstration by Foster and Cort (1932, 1935) that dogs immunized by repeated light infections were rendered again susceptible, i. e. non-immune, when thereafter fed this same deficient diet. They carried the experiment a step further and showed that when such "deimmunized" dogs were restored to the balanced diet they reacquired, or perhaps more accurately, reactivated, their immunity and actually discharged the anemia producing worms they had acquired while on the deficient diet.

Such experiments as have just been described do not permit one to determine which of the nutritional elements bear a specific relationship to the capacity of the host to combat the worm infection. It seems evident (Otto and Landsberg, *loc. cit.*) that whatever, if any value, iron salts alone have in the prevention of the anemia, they have no demonstrable value in enhancing the hosts, capacity to develop immunity. Because of the expense in time, money, and space we have made no attempt to analyze the dietary constituents in relationship to immunity in dogs. However, comparable studies have been carried out in this and other laboratories with smaller laboratory animals. Vitamin A deficiency has been shown to adversely affect the capacity of rats to combat a number of nematode infections effectively (*viz.* Spindler, 1933; McCoy, 1934; Lawler, 1941; Riley, 1943; Watt *et al.*, 1943). The several elements of the vitamin B complex have been less extensively considered, but they also have been shown to reduce the resistance to nematode infectionst(Ackert and Nolf, 1931; Watt *et al.*, 1944).

A number of these diets, in which vitamin content has been primarily considered, have unavoidably had deviations from the normal protein, either in amount or type of the essential amino acids. Furthermore there was an almost complete absence of protein from the generally deficient diet used in the hookworm experiments described above. Accordingly, the effect of the protein deficiency upon immunity has been the subject of our most recent studies (Donaldson and Otto, 1946) in experiments utilizing the laboratory rats and *Nippostrongylus muris;* the latter is a fairly close relative of hookworms and a normal parasite of rats. In these experiments the only sources of animal protein, casein and whole milk powder, in the balanced diet were replaced by cornstarch and slightly increased amounts of yellow corn meal and whole wheat flour to produce a deficient diet. Vitamin content and salt balance were maintained by increases in butter and inorganic salt content. Thus the only discernible differences between the balanced and the deficient diet was in the protein content. The balanced diet contained approximately 22% protein, 14% animal and 8% plant protein, whereas the deficient diet contained no animal and only 9% plant protein; carbohydrate (corn starch) replaced the 13% protein removed from the latter.

Only slightly more worms developed from the initial infections in the animals on the deficient diet than in those on the balanced diet. However, the animals on the balanced diet expelled most of the worms in less than two months whereas those on the deficient diet discharged very few of the worms during this period, i. e. no demonstrable immunity developed during this period. In a second group of experiments, involving 60 rats, a series of immunizing infections were given both to rats on the deficient diet as well as to their litter mates on the balanced diet; those on the balanced diet became immunized and harbored only about 25 worms each at the end of the experiment whereas those on the deficient diet harbored 570 worms each. Thus the latter failed to develop the highly protective immunity; nevertheless, they were not completely susceptible since the 570 worms represented scarcely more than 10% of the larvae administered. In another set of experiments, in-

volving over 50 animals, rats were immunized by repeated infections; after immunity was verified, one-half of these animals were placed on the deficient diet. After 36 to 60 days on the protein deficient diet, both groups and a third non-immunized group on the balanced diet were given challenging doses of 1100 and 1200 larvae (the doses differed in different experiments); the animals were killed 12 and 13 days later. It is evident (table II) that the immunized animals had lost much of their immunity after being on the deficient diet as short a time as 36 days. However, they still had an appreciable degree of immunity at the end of 60 days since they harbored much fewer worms than non-immunized animals.

We visualize that something comparable to this occurs with dogs or humans suffering repeated exposure to hookworms while being partially debilitated by dietary deficiencies. If they are not killed by immediate blood loss they may develop some degree of immunity but not sufficient to throw off the worms and chronic hookworm disease results. Thus I am convinced that chronic hookworm disease does not have a single etiological agent but rather the worms can maintain themselves only when the host is already debilitated and the worms in turn contribute to the debilitation and a vicious cycle it set up. While protein deficiency undoubtedly prevents the development of a highly protective immunity, it is equally true that certain other deficiency states, such as vitamin A deficiency, likewise interfere with the development of immunity. Epidemiologically, malnutrition is associated with hookworm disease of man and it seems equally true of hookworm disease of dogs.

It seems to be altogether likely that dietary deficiencies may well be a contributing factor, to a degree not yet fully appreciated, in the failure of a host to protect itself against other infections. In this connection it is of more than passing interest that we have never had a pyogenic infection in the exfoliated areas of the skin of the immunized dogs when such dogs were on the normal stock diet. On the other hand such pyogenic infections commonly occur in the skin of the dogs debilitated by dietary deficiencies.

TABLE II.—SHOWING THE LOSS OF IMMUNITY TO NIPPOSTRONGYLUS MURIS ALREADY ESTABLISHED BEFORE THE HOST WAS FED THE PROTEIN DEFICIENT DIET; SUMMARY OF THREE EXPERIMENTS INVOLVING OVER 50 RATS

Days on Deficient Diet	No. of Larvae in Test Infection	Immunized and thereafter: Placed on Deficient Diet	Immunized and thereafter: Maintained on Balanced Diet	Non-immunized Controls on Balanced Diet
36	1100	149	11	536
38	1200	107	8	721
60	1200	208	15	531

Age in Relationship to Immunity

It has been amply demonstrated with a wide variety of nematode infections in a number of different hosts that mature hosts will tolerate much heavier initial infections than will young animals. Thus 500 to 1,000 hookworm larvae will kill a newly weaned puppie whereas an animal four months of age will tolerate several thousand and a year old dog will often tolerate 10 to 20 thousand and we have had them tolerate over 50,000. In all such animals, old or young, the initial infection shows a high percentage development followed by a rapid elimination of the worms, the older animals eliminating them more rapidly. Thus it seems to me probable that the older animal with its wider antigenic experience is able to respond more rapidly to a new such experience, viz. its initial infection with hookworm.

General Discussion and Practical Considerations

Since the general conclusions which we have arrived at from these studies have already been presented under four main headings in the introduction it remains only to indicate how these considerations may be harnessed into practical application for veterinarian and the dog owner.

Although a highly protective immunity is established as a result of infection no attempt, so far, to induce such an immunity with whole dead worms or extracts of worms has been successful. Some measure of protection has been obtained in some cases by subcutaneous injection of hundreds of thousands of heat killed larvae several times a week over a period of five months. But the results were not consistent. It would appear that the protective response is stimulated by the metabolic products of the living worms rather than by the chemical constituents of the worms themselves. Accordingly, there is no readily available, or even early anticipated, method of routine protection by artificial immunization. Likewise although the serum of immunized dogs con-

tains a substance highly toxic for the invading larvae, there is no evidence that such serum would be of value in amounts which it is practical to administer. It seems evident then that these studies and conclusions derived from them can be of immediate practical value only in so far as they point the way to the best utilization of the naturally developing immunity.

Attention should be called to the fact that single exposures of 50,000 to 1,000,000 larvae, such as were used in challenging the established immunity in these experiments, rarely occurs in nature. Accordingly, the immunity established under natural conditions would probably not be subjected to such drastic challenge.

It is important to remove the hookworms from a heavily infected dog, whether such a dog is young or old, whether suffering from acute or chronic infection.* However, to assume that the removal of the worms was getting at the basis of the problem would be erroneous in most cases. Considerations should be given both to the nutritional status of the animal and the opportunities for immediate heavy reinfection. Concerning the diet it probably is a mistake, by and large, to prescribe the vitamins and iron with abandon without giving careful thought to other possible nutrient factors. Of these, proteins, particularly proteins of animal origin, are extremely important. If meat, including both liver and muscle with bone, and vegetables are included in the diet, both iron and vitamins as well as protein will be supplied in ample quantity for most needs. If the anemia is pronounced, supplementary iron may be helpful and if malnutrition is pronounced, vitamins may be helpful, but only if the protein (and a salt balance) is adequately supplied. To prevent re-exposure to immediate heavy infections it is necessary only to remove the animal from its previous defecation sites on moist soil or similar defecation sites of other heavily infected dogs.

To attempt complete protection of the animals is probably futile and nominal exposure will provide sufficient immunity to prevent serious disease. It is necessary then primarily to protect the young puppies which are the principal victims of acute heavy infections. Here the veterinarian's advice to the owner is extremely important. The veterinaian and kennel operator should consider whether or not the hazards of close confinement in his kennels have been adequately balanced by sanitary precautions. Law (1933) and Sprehn (1937) have emphasized how hookworm infection is a comparatively harmless infection in wild foxes, but becomes economically a very important disease, causing severe debilitation and often death of the fox pups, under conditions of confinement on fox farms in Canada, Northern United States, and Germany. It has been emphasized by these workers, Sweebe, Shillinger, and others that common sense application of nominal concepts of sanitation will be excellent protection for foxes even under necessary confinement on fox farms. The principles utilized in evolving the McLean County System of controlling ascariasis in swine (Raffensperger and Connelly, 1927) are applicable here as the most effective method of preventing critical hookworm infections (and ascarid infections as well). Reduced to simplest terms it means whelping the pups and maintaining them during the suckling period under sanitary conditions. With swine this is accomplished by isolating the sow in a freshly scrubbed farrowing pen three or four days before farrowing. Before she is isolated, all loose straw and any other grossly adherent debris is brushed off and the udders washed with soap and water. The suckling pigs are not allowed to leave this pen, which is maintained fairly clean, until they are transported to clean pastures. Not until they are three to four months old are they permitted to go into the permanent hog lot. The conditions of confinement in swine husbandry make it appear that this offers fewer problems than with dogs but actually such is not the case. Ideally from the standpoint of worm prevention, such confinement of the whelping bitch and her pups would appear indicated when feasible. Wooden or concrete run ways which can be cleaned with water are ideal; steam or boiling water is to be preferred but well washed pens with daily exposure to the direct rays of the sun will provide adequate protection. Even earthen runways are safe if they are dry and sunlit and not used for a month or longer before by infected dogs. Moist, shaded earthen runways or areas under houses where dogs congregate offer the greatest hazard. It is probably simpler to avoid the use of such runways than undertake their treatment but it is possible with the use of salt brine to effect some measure of control. It is necessary to sprinkle nearly a quarter of pound of salt, as a brine, on every square foot of soil and then the protection afforded is only temporary. The screen floor runways, so effectively used in some fox farms, also seems unnecessary for dog kennels under most circumstances.

*For this purpose we have found tetrachlorethylene completely satisfactory when administered per os in soft gelatine capsules after 12 to 24 hours starvation. We have varied the dose around 0.1cc per pound of body weight, using a lower dose for puppies than for mature dogs; thus a 15-pound young puppy of a large breed of dog would receive 1.0cc or even less whereas a mature 15-pound Boston Terrier would receive 2.0cc although the exact computation at $.1cc per pound would be 1.5cc for either animal.

Although worms established in the alimentary canal cannot directly infect pups, they do provide a supply of eggs for seeding the defecation sites and if the bitch is confined to a runway where she will later whelp and raise her pups she may well be creating a hazard. Accordingly nothing is lost and much may be gained by worming the bitch before she is bred. While the worms already established cannot migrate to the pups during pregnancy, nevertheless, prenatal infection can take place when the bitch is exposed to reinfection during pregnancy; Foster (1932, 1935) has shown experimentally that as many as 10 to 20% of the infective larvae administered to a bitch during pregnancy may ultimately develop in her pups. Accordingly it is desirable to reduce exposure to infection during pregnancy.

How to Avoid Ancylostomiasis

It cannot be emphasized too often that complete elimination of exposure to infection is not necessary but rather it is important to prevent *gross exposure* to infection. Nevertheless, the author has experienced no difficulty in repeatedly raising Boston Terrier puppies, under ordinary surburban household conditions, free of worms until weaning time. Any hookworms or ascarids were removed with tetrachlorethylene before breeding the bitch. During pregnancy she was allowed free, but not unrestricted run in the neighborhood where dogs were common. A few days before whelping time she was bathed and thereafter allowed exercise only in the house, clean runway, or on a leash until the pups were whelped. During the suckling period she was again allowed some free, but not unrestricted, run but she was bathed at intervals and the pups were never allowed to suckle if there were obvious layers of dirt on the udders. The pups themselves were confined in the basement and to a partially shaded and partially sunlit runway in which no heavily infected dog had ever been confined. After weaning, immunity developing from nominal exposures was expected to provide suitable protection. Worming a lightly infected, healthy dog which will continue to be exposed to infection is, in my opinion, completely futile.

Summary

Evidence is presented that sublethal infections with the hookworm, *Ancylostoma caninum,* stimulates a highly protective immunity. Well nourished animals may become acutely anemic or even die if the initial infections are extreme, but if they recover they are thereafter refractory to reinfection. Mature animals respond immunologically much more rapidly than puppies and accordingly tolerate heavier initial infections. Malnutrition, such as results from protein or vitamin deficiencies, seriously impairs the animals capacity to develop immunity and may dissipate an already established immunity. Attention is directed therefore to a consideration of the nutritional status of a dog suffering from clinical hookworm disease. A distinction is made between mere hookworm infection and the heavy infection which produces disease. The latter is primarily a problem in young puppies under conditions of poor sanitation. Practical procedures for preventing the disease in puppies are discussed.

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Mysterious Ailments in Animals

Every practitioner knows that the variety of conditions in livestock for which his services may be asked is almost endless. Determining the cause of loss in farm animals frequently confronts him with a first-class mystery. Poisoning in animals, as in detective yarns, is a prolific source of puzzlers. Usually it is not sufficient to arrive at a diagnosis such as "lead poisoning" or "forage poisoning" or "pitch poisoning" etc. from the symptoms and postmortem lesions. To prevent further disaster to his herd the owner of the animals wants to know, and needs to know, where and how they obtained the poison. Answering this question often involves ingenious methods and skill.

In the March bulletin of the Eastern Iowa veterinary association several unusual cases occurring in the practices of members of the association are given.

1. Sudden losses had occurred, at irregular intervals, over a considerable period, in a herd of swine. These animals were fed ashes from the home fires regularly. Smoke from the parlor stove passed through a long section of horizontal stove pipe. It was necessary to burn "soot remover" in this stove from time to time to maintain a draft. Patient inquiry and examination of records finally revealed that it was only when ashes were fed following the burning of soot remover that hogs died.

2. Thirty brood sows and shotes were affected with the symptoms of "salt-poisoning." It required insistent questionign to get the It required insistent questioning to get the a cupful" of brine from some cured meat.

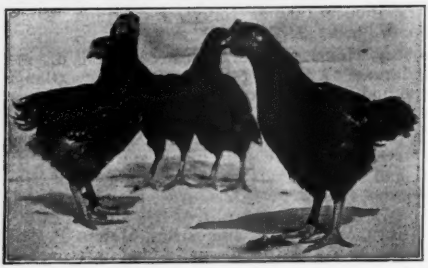
3. Frost melting on the underside of a galvanized roof drained into a bunker containing rock salt and dripped from one corner of the bunker to form a very small pool from which some young pigs drank with unhappy result.

4. A thrifty drove of heavy shotes, suddenly ceased to eat and began to cough. A kindly neighbor suggested mineral oil. Disaster followed and it was almost by accident that it was discovered that fuel, not mineral oil intended, had been given.

5. In a number of cases swine died after being smeared with crank-case oil as a mange treatment. The lesions indicated lead poisoning. The source of the lead was determined only by learning that only ethyl gasoline had been used in the motor.

6. Young pigs affected by both pox and lice were dipped in a commercial dip to kill the lice. It killed the pigs too—cresylic acid poisoning. Apparently the pox lesions were responsible for absorption of an undue amount of the dip.

7. On another farm a diagnosis of forage poisoning in cattle was met with the challenge that the feed, both grain and hay was of the best quality. But on examining the hay it was found to be piled on a two-year old butt of spoiled sweet clover hay. There were many burrows where the cattle had worked their heads through the good hay to reach and eat the sweet clover. Several fatalities resulted.



Examination of Dressed Poultry for Decomposition

By H. D. PRITCHETT, V.M.D.
Farmville, Va.

IN another paper[1] it was pointed out that improper slaughter is a definite forerunner of premature decomposition frequently occurring in dressed poultry while in transit or otherwise in a commercial status. The objective of this paper is to place before the reader certain criteria upon which to base a diagnosis of decomposition encountered in dressed poultry inspection. Since the type of decomposition most frequently observed in this food product appears to be a subject of a controversial nature, the writer's purpose in presenting this paper for consideration is to suggest a basis upon which to standardize the method of determining visually, and by the usual post-mortem procedures, the presence and extent of decomposition occurring under commercial conditions in this item of human diet.

Regardless of the controversies as to the wholesomeness or unwholesomeness, even possible danger to the physical well-being of those individuals who inadvertently consume questionable foodstuffs, decomposition occurring in different forms and degrees must of necessity be carefully considered when passing judgment on the edibility of any food product. Especially in connection with poultry it would appear that the examiner must, along with other extensive knowledge, be intimately familiar with the manufacturing (dressing) processes commonly applied to the preparation of poultry for market, location of sources and of the ultimate consumer, and usual practices of transportation and refrigeration while in transit. Without this basic information, it would seem to be difficult, if not altogether impossible, for the examiner to arrive at a valid conclusion as to the progenitors of the type or degree of decomposition that may be present, constituting a very important phase of poultry inspection. It is also of course necessary that the examiner be capable of recognizing decomposition, but it is equally as important that he know the causes and approximate sources of the occurrence of the type of decomposition under consideration.

Of course, no particular problem arises if the degree of decomposition which is easily recognized by almost any individual were the topic for consideration; but that is not the case, because this advanced form of decomposition is rarely if ever a matter for consideration. At least, this type of deterioration obviously presents no special difficulties to the experienced examiner. It is not the grossly putrid, vile-smelling cadaver[2] which is easily dismembered due to autolysis, that is of primary concern; but the early and primary stages of spoilage, which are most likely to prove troublesome to the examiner in exercising conscientious judgment. Therefore, one placed in a position demanding such accurate judgment should first be fortified with intimate knowledge of the causes of spoilage of this type of food product, and be prepared to substantiate his opinion, based on technical knowledge and experience rather than his own theory alone.

Eliminating this very extensive protein disintegration, only those conditions of spoilage which are commonly seen will be discussed. In so doing the reader must constantly keep in mind the extremely potent factor of human fallability and individual idiosyncrasies, pertaining to the exercise of judgment and interpretation, which is an ever-present problem. Sensitivity of perception, and response to the various types of odors encountered varies within considerable latitude in individuals; and many persons are known to be totally unable to detect certain odors that are quite evident to other individuals. It is therefore readily apparent that judgment of decomposition in dressed poultry, is dependent upon much more than elementary knowledge. A broad experience under the tutelage of one endowed with the ability to detect and differentiate odors and shades of discoloration, would seem to be one of several required essential prerequisites for this work. There also appears to be considerable reason to suspect that many individuals are hopelessly incap-

able of differentiating colors commonly seen in dressed poultry. It has been noted that more than a goodly percentage of consumers do not recognize the normal color of a chicken carcass; consequently, such persons could hardly be expected to recognize a carcass or cadaver presenting abnormal discolorations. These hapless individuals are entirely dependent upon the integrity and ability of the expert poultry examiner to maintain vigilance and safeguard the wholesomeness of their supply. Any examiner can locate certain retail distributors where one can watch housewives buying over the counter poultry which is green-struck, slimy, smelly and grossly discolored. The writer did on an occasion do exactly this, and while observing in wonderment what housewives were buying for food at a bargain counter, was confronted by a kindly elderly lady who said (and I quote), "Mercy sakes alive, don't these people know that those chickens are not fit to eat!" To lead her on to further commitments the writer replied, "Why, what's the matter with them?" She replied, very venomously, "Young man, my father was an undertaker, and I know what it means when a body turns green just like these chickens." By this time a clerk had accosted her and led her away to another counter and, incidentally, better chickens. The lady had many years ago learned in the "embalming room" what green discoloration meant; and it can be stated here that the particular chickens to which she referred were indeed very poor subjects for "embalming," yet they were being purchased for food.

It is not intended that a discussion of the possible dangers to human health from the consumption of decomposed meats be entered into, but an attempt will be made to describe in some detail the more salient features upon which the basis of a diagnosis of decomposition is believed to be dependent, leaving the argument of edibility of decomposed meats to those who have no objection to the unwholesomeness of the meats they eat, although state and federal laws declare that foods decomposed "in whole or in part" are unfit for human consumption. Thus, it will suffice to first divide dressed poultry into the following six classes. While for the purpose of the paper in hand such a division may possibly appear irrelevant, nevertheless a full understanding of the types of dressed poultry encountered routinely would most certainly appear to be pertinent in assisting one to evaluate more accurately the actual state of preservation and the causes augmenting deterioration of the several marketable styles of prepared poultry most commonly seen. However, this classification is in no way presupposed to be complete, neither is this paper offered as an exhaustive treatise of the subject.

Market Classes of Poultry

1. Fresh Dressed: sometimes referred to as New York dressed, hog dressed, city dressed, in-the-round, and no doubt other designations according to geographical locations; consisting of the bled carcass with feathers removed; head and feet may or may not be removed. The carcass may be packed either dry or wet in barrels, boxes, crates, baskets, etc., with cracked or flaked ice, or box packed without ice after having been precooled, but not frozen.

2. Fresh Dressed, Sharp Chilled: same as fresh dressed, but not solidly frozen. The muscles are firm and well set, the joints offer considerable resistance to manual flexion. Usually box packed, wrapped or unwrapped, and without ice. Ice crystals may be palpable in the heavy muscles and body cavities. The color will be somewhat darker than that of the carcass simply cooled but not sharply chilled.

3. Fresh Dressed frozen: same as fresh dressed, either wrapped in paper, etc., or unwrapped, packed in barrels, boxes, crates, etc.; solidly frozen, either with or without ice. The color will be considerably darker than the sharply chilled and unfrozen carcass.

4. Eviscerated: viscera removed (usually the head and feet removed, but not always) sometimes referred to as "full drawn" or simply "drawn." Modifications of full drawn or eviscerated are known as "Boston drawn" and "wire drawn," the latter method a modification of "Boston drawn," designating an operation of incomplete evisceration, for which there are several technics. The latter two methods of evisceration are insanitary. Deviations such as these from legitimate evisceration contribute greatly to the contamination of the finished product with fecal material, and therefore materially facilitate decomposition. Evisceration, and the modified methods, unless the operation is performed and supervised by veterinarians, preclude any efficient system of inspection from the disease viewpoint. This writer advocates veterinary inspection of all operations concerned with dressed poultry, and believes that this supervision should be directed toward the principles and best interests of the public health, rather than those of commercial or economic origin.

5. Cut Parts Poultry: as the term implies, the dressed carcass is dismembered into its several edible components, and sold separately according to consumer demand. This product may be encountered either dry or wet packed with ice, frozen, sharply chilled, or merely iced. Usually packed in a wide variety of packages, many of which are entirely unsatisfactory so far as sanitation is concerned. This type of poultry defies the ingenuity of the examiner, because it is possible to so manipulate it as to almost completely mask primary spoilage, or at least render its detection extremely difficult by usual methods of examination. It is also possible to prepare diseased poultry in this manner; therefore, poultry in this form should be prepared only under veterinary supervision, and rigid supervision should

be constantly maintained over establishments offering this type of poultry to the consumer.

6. Miscellaneous Forms: includes other types of preparation such as eviscerated or uneviscerated but vacuum packed, wrapped in cellophane, packed in sealed packages; also other forms materially differing from those hitherto described, such as "spreads," "patés," dehydrated, smoked, pickled, "chicken-burger," "a la king," canned, soups, and possibly others.

Poultry Inspection Procedures

Poultry inspection really embodies two separate procedures: the first being sanitation of the dressing plant, efficiency of the various operations, cooling and packing processes, and the condition and state of health of the birds being slaughtered; and secondly, that phase of inspection of primary concern at the moment, which is confined to the point of destination or distribution. Here the examiner can concern himself only with the actual condition of the poultry, the presence or absence of evidences of disease, and sanitation of methods of handling and/or processing.

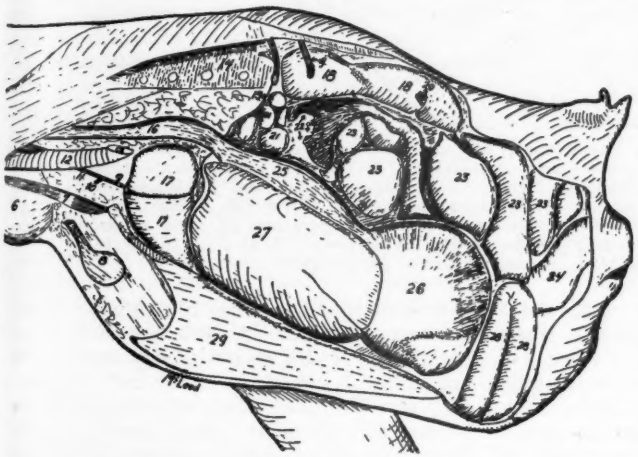
In the case of frozen poultry, examination for the detection of the type of decomposition being discussed should never be made for several reasons, the most important of which is: in frozen birds it is for all intents and purposes impossible to detect decomposition odors and to differentiate definitely between alterations of color which generally accompany the various stages of objective decomposition, all of which may be materially altered by freezing. Decomposition as it is usually encountered may originate from the exterior of the carcass and be manifest by the presence of a palpable slime and abnormal colors and odors. On the other hand, visceral decomposition may be well advanced yet, strangely enough, not be objectively visible externally. Extensive visceral decomposition occurs in many carcasses in which, frequently, no positive indications of decomposition can be detected by casual external observations. Since it is important that odor be perceptible, and deviations of color of the carcass from normal be demonstrated, it becomes necessary that the birds, to be examined for decomposition and disease, be at least partially thawed or "sweated" and softened considerably, although heavy muscles, viscera and body cavities may contain some palpable ice crystals. Nevertheless, even this degree of thawing may on occasion be found entirely inadequate to permit the perception of decomposition odors; therefore, complete thawing may become imperative. As extensive thawing of frozen poultry degrades the birds commercially to an appreciable degree, no more than is absolutely necessary to constitute a fairly representative portion of carcasses should be thawed or sweated. On the other hand, one should not hesitate to thaw what is believed to be a suitable number of birds for fair and thorough examination. The examiner should also constantly bear in mind that once poultry has been frozen (either with or without the viscera) and then thawed, its keeping qualities have been seriously impaired. It has been demonstrated that dressed poultry "in the round" will, under equal conditions, keep fresh and wholesome for a longer period than eviscerated poultry. All consistent haste should be employed, but never for a moment forget that haste begets inefficiency and error. Should it become necessary to thaw frozen poultry, considerable care and good judgment must be exercised by close observation of the degree and extent of thawing, which should be done under slow conditions at approximately room temperature if possible. Too rapid elevation of the temperature appears in some cases to hasten the formation of a sticky and slimy condition of the carcass, easily detected by manipulation. This slimy condition must not be confused with the condition referred to by the industry as "oily," which is usually due to extravasation of fat from the carcass of heavy fat fowl. This "oily" condition may be the result of breakdown of the adipose tissue by decomposition, in which case differentiation would simply be a process of elimination of odor or detecting its presence. Carcasses presenting this "oily" exterior appear to be wet and of course greasy; while the slimy condition is the result of spoilage bacteria and visually appears glistening, moist and very slippery, leaving the hands sticky and smelly after handling. While the greasy exterior and the slime of spoilage can be removed by washing and other treatment, the examiner must be very cautious that he does not pass for food consumption birds that are undergoing spoilage. It is not entirely impossible for this "oily" condition to be erroneously judged as a phase of decomposition that preceded freezing. To differentiate, good judgment and considerable experience appear to be necessary.

Examination of Frozen Poultry

For examination purposes, frozen poultry should never be thawed in water, as this method of thawing will obviously remove or camouflage evidence necessary in the judgment of decomposition in the form of slime, odor, and alterations of color due to bleaching. Frozen poultry, if and when it should appear necessary to thaw in water for pur-

poses other than examination, must be very promptly distributed for consumption, or immediately processed, as deterioration is extremely rapid. This method of thawing presents serious sanitary problems, because an appreciable amount of water that may be extensively contaminated with fecal material, etc., will gain access to the interior of the carcass and consequently be absorbed. Much poultry that was frozen one or more times is sold to the retail trade after thawing by this method, which might very easily be one of the major causes of the spoilage frequently seen. During the thawing process preparatory to examination, frozen poultry must be protected at all times from exposure to high temperature, direct sunlight, forced drafts which cause rapid and excessive dehydration, rodents, insects and other predatory animals, as well as molestation by curious or malicious persons which might seriously interfere with positive identification of the material undergoing examination. It is also extremely important, to protect the interests of all parties concerned, that almost constant surveillance be maintained to observe the degree of thawing so that the examination can proceed with all expediency and efficiency immediately upon the birds attaining a suitable condition with respect to thawing, permitting a thorough examination, both visually and by autopsy; the latter operation being necessary not only for the demonstration of pathological processes and parasitological infestations, but for the detection of visceral decomposition as mentioned above.

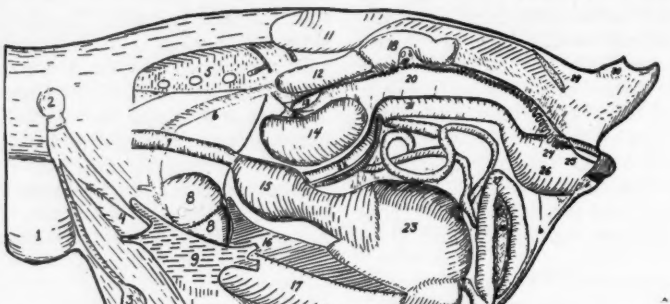
Post-mortem examination of the carcass of course begins with a visual examination of the entire external aspects, and one should especially note the method and efficiency of slaughter employed. Observations should be made of the color and odor of the carcass, and the presence or absence of slime should be determined. Extreme dehydration and shrinkage of the eyeball may often indicate that the bird had been slaughtered for a considerable period, although frozen carcasses will sometimes present these characteristics after thawing. Cyanosis of the combs, wattles and ear lobes, and occasionally the mucous membranes of the eyes and mouth, may indicate slow asphyxiation. This feature is also present in carcasses of birds suffering from disease at time of slaughter. The head and mouth should be carefully examined for decomposed blood and the carcass must be found to be clean at all times. The cloaca should be examined to ascertain the presence or absence of fecal material, which should have been expressed (manually, or mechanically by the buffer) while in the process of dressing, prior to the last washing. Failure to perform this operation often results in extensive contamination of the carcass with fecal material in packing and/or transportation. Such a condition facilitates and contributes to early spoilage of the carcass and promotes the condition known as "green-struck" in region of the vent. A fresh, healthy carcass is firm and the muscles are solid. The joints will be fixed and offer considerable resistance to manual flexion. Always regard a soft, flabby carcass as possibly decomposed, until it is demonstrated to be otherwise. A thorough external or visual examination having been made of a number of carcasses, one should proceed to examine a number of carcasses internally. The technic of autopsy for purposes of detecting decom-



Viscera of the female chicken, lateral view. 6. Crop. 7. Sternotracheal muscle. 8. Hypocleidium. 9. Brachiocephalic artery. 10. Brachial artery. 11. Carotid artery. 12. Syrinx. 13. Bronchus. 14. Ventral spine—thoracic vertebrae. 15. Thoracoabdominal diaphragm. 16. Esophagus. 17. Heart. 18. Kidney. 19. 7th rib. 20. Ischiatic artery and nerve. 21. Ovarian follicle. 22. Infundibulum. 23. Oviduct. 24. Colo-rectum. 25. Glandular stomach. 26. Muscular stomach. 27. Liver. 28. Duodenum. 29. Keel of sternum

position should be systematic and equally as thorough as for the purpose of diagnosing disease.

On opening the abdominal cavity in the usual manner, it will sometimes be noted that the abdominal walls immediately collapse and a rush of foul gas is frequently heard when the knife puncture is made. Such a carcass is usually extensively decomposed internally. Decomposition of the viscera is manifest by a wet, soft, flabby feeling when touched, and a variety of colors will be noted. There may be extravasation of bile throughout the liver and adjacent tissues, due to breakdown of the gall bladder and liver. The viscera will have lost their natural tone and will be a mass of soft, mushy material that ruptures easily on manipulation or extirpation. Odor is of course very definitely present. For practical purposes such findings would condemn as unfit for food such a carcass, but the thorough examiner is justified in going further by exposing the joint cavities. The natural body fluids in a dead body are in a more or less constant state of motion by passage to and from individual cells; consequently the products of decomposition are picked up, and in some cases, such as the joint cavities, this fluid, bearing odoriferous evidence of decomposition, is deposited in these natural reservoirs. Thus the larger joints such as the coxo-femoral articulations and the spinal canal, exposed by luxation, will demonstrate the presence of decomposition by odor long before the actual visceral alterations occur visibly. The scapulo-humeral articulations of large birds should also be likewise invaded, and the pectoral muscles of heavy birds should be examined for odor by slicing off sections. A decided odor of decomposition will often be detected in spite of the apparent normal appearance of the muscles; and such muscles when boiled will usually clear up any existing doubt in the mind of the examiner. For this reason any poultry that is not edible as such, is obviously unfit for canning or other processing; while on the other hand some such poultry meat may be suitable for immediate processing and sterilization, yet entirely unfit for shipment, freezing, or other handling with the object of being utilized for food. A carcass presenting a distended or bloated abdomen should always be regarded with considerable suspicion, and the examiner must be on the alert constantly that he is not adversely influenced in his judgment of decomposition by interested parties on the grounds that the obvious odor is a "natural chicken odor." One must learn to differentiate between odors of decomposition, and the natural odors of normal fat[3] and other normal body tissues and fluids. Abdominal odors will invariably result from decomposition, as well as from certain aromatic foods eaten.



Viscera of the male chicken, lateral view. 1. Crop. 2. Glenoid cavity. 3. Hypocleidium. 4. Coracoid bone. 5. Ventral spine—thoracic vertebrae. 6. Aorta. 7. Esophagus. 8. Heart. 9. Sternum. 10. Keel of sternum. 11. Ileum. 12. Kidney, anterior lobe. 13. Epididymus. 14. Testicle. 15. Glandular stomach. 16. Liver, cut surface. 17. Liver. 18. Kidney, middle lobe. 19. Ischiatic artery and nerve. 20. Mesentery. 21. Large intestine. 22. Small intestine (cecum just below). 23. Muscular stomach. 24. Ductus deferens. 25. Ureter. 26. Rectum. 27. Duodenal loop. 28. Pancreas. 29. Ilium. 30. Glandulae uropygii.

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Fatty Degeneration of the Liver in Mink

By T. T. CHADDOCK, M.S., D.V.M.
Grafton, Wisconsin

A CONDITION characterized by the deposition of light colored fat in the liver is seen in mink of all ages and all types; at all seasons of the year and in all sections of the North American continent where ranch bred mink are raised in any considerable numbers. Both sexes are involved but due to the physical stress of raising young, the condition is seen approximately twice as often in females as in males. It is non-infectious and thought to be nutritional in origin and, on occasions, heavy losses are suffered on some mink ranches.

Mink ranchers and some investigators have called this ailment "yellow fat." That name is ill chosen since deep colored fat is common in emaciated animals whatever the cause, and to name an ailment for this lesion, can but lead to confusion. Yellow fat is a condition entirely different from inanition. It is nutritional, characterized by orange colored fat deposits in the liver. This ailment is signalized by lesions, chiefly microscopic in many tissues, but the most important one, other than a deep colored fat, is a replacement of liver cells by globules of fat. Fatty degeneration of the liver is believed to be the ultimate cause of death from the disease and hence would seem an appropriate name for the ailment.

I have observed this condition but twice in wild caught mink, but have seen it in specimens of ranch mink from every state in which fur bearers are raised. The investigations here recorded were made mainly during 1943 and 1944. Complete microscopic studies were made on 100 typical cases of this condition. The following report gives the results of that study and also observations of the ranch where I had complete control of matters concerning the health of the animals. My recommendations were followed to the letter and accurate reports were always available.

In 1943 the ranch contained 1,981 mink, of which 1420 were kits and classed as young, and 561 were classed as adults. Of the adults, 330 were born on the ranch, while 231 were purchased from outside sources.

Details of the ailment on this ranch given for 1943 and 1944 are listed in Table I. It will be noted that the loss in 1943 was slightly in excess of 8%; in 1944 it was approximately 20%. An overall loss of 20% is more than any rancher can withstand and still remain in business. The normal loss on a mink ranch runs around 3 to 5%.

Fatty degeneration of the liver, like other ailments due to nutritional derangement, strikes hardest when abetted by some other factor or factors which increase the stress to which the animal is subjected. In this instance exposure to inclement weather and the devitalizing effect of gestation, parturition, and lactation increase the mortality from fatty degeneration of the liver.

TABLE I.—MORTALITY AND SYMPTOMS DUE TO FATTY DEGENERATION OF THE LIVER IN MINK ON A FUR RANCH IN 1943 AND 1944

Year	Mortality* Male†	Mortality* Female†	Gastric Ulcers Male	Gastric Ulcers Female	Cystic Calculi Female
1943	55	107	2	4	5
1944	116	286	34	96	15
Total	171	393	36	100	20

*The months of greatest death losses in 1943 were March (28) and October (31); in 1944, March (141), April (54). Losses were increased by (1) very hot weather, (2) very cold weather and (3) long exposure in wet weather.
†The seasons of greater death losses were: In males, mating; in females, whelping, nursing, weaning.

Etiology

The true causative factor is not definitely known. Observations made of the different experiments strongly indicate that this condition is noninfectious and occurs only in animals that are fed an unbalanced diet. By this it is meant that the diet made up of the various ingredients was either too concentrated or did not contain the necessary ingredients in adequate amount for the nutritional requirements of mink. Most of the feeds examined were lacking in bulk, and when greater bulk was provided the trouble stopped.

Symptoms

Some of the affected animals appear to be in good condition; others are greatly emaciated. There is listlessness, inappetence and little activity. Affected mink remain in the nest box most of the time.

The quality of the fur is poor in some cases; in others it appears to be unaffected. A definite bar has been observed in the underfur in apparently healthy mink on the same diet. Any mink that has been ailing will show this bar. Diarrhea is usually present. Shortly before death the animal becomes comatose or the end may come in convulsions. Male mink die in the greater numbers during the mating season or while being caught.

Lesions

The mesenteric fat may or may not be of an amber color. In some cases there are visible globules of fat floating in the ascitic fluid. Fatty degeneration of the liver is constant but may vary in degree, depending upon the stage of the ailment in which the liver is examined. Ulceration in the pyloric region of the stomach is nearly always present and in some cases to such an extent that there is a perforation of the gastric mucosa. The intestinal wall is thickened and shows little tone; the contents are muco-hemorrhagic.

Degeneration of the kidneys is common. Secondary pneumonia is usually present. The heart is enlarged. In the pregnant female the fetuses are usually mummified. Rupture of the uterine wall was observed in several instances, allowing the fetus to pass into the abdominal cavity. Peritonitis develops shortly afterwards in these cases. Rupture of the liver is common and usually caused by handling or the exertion of mating. There is rapid loss of flesh. Animals that survive for any considerable period are emaciated. Cystic calculi have been observed in several of these animals but are probably not significant. The costal cartilages at the symphysis of the ribs in many instances have a distinct enlargement. The gall bladder is often distended and on opening will yield small sandlike crystals. The bile is usually abnormal in color and the ductus choledochus is usually patent.

Microscopic Lesions

In the central nervous system there is a great amount of congestion and even rupture of the blood vessels of the pia mater, dura mater and arachnoid. There is convolution of the blood vessels of the medulla with some degree of thickening of the intima. Degeneration of the brain cells to such an extent that liquefaction occurred was often observed.

The heart showed an extensive amount of proliferation of the organ which was probably compensatory. Hemorrhage between the fibers of the myocardium and degeneration of these fibers with traces of calcification were noted.

In the lungs, all stages of pneumonia were observed. Cicatricial tissue formation in the walls of the alveoli, necrosis of the alveoli due to the development of foci of infection, degeneration of the medial and external walls of the arteries and veins of the bronchi, small areas of emphysema and edema—all were seen.

There were hemorrhages in the mascularis and secretory mucosa of the stomach and partially digested red blood cells were present on the surface of the gastric mucosa. The entire gastric mucosa was affected by degeneration which decreased the tone of the organ.

The intestine had extensive hemorrhages between and in the villi and between the fibers of the circular and longitudinal muscles. Much mucus was present between the villi.

In the liver there was fatty degeneration of the hepatic cells, hemorrhages between them, with focal necrosis involving many of the cells. Within the hepatic cells most of the cytoplasmic material had been replaced with adipose tissue and the nucleus was crowded against the wall of the cell to such an extent that it was greatly deformed and probably no longer functional.

There were a few areas of degeneration in the walls of the splenic arteries, otherwise the organ appeared to be normal.

In the kidney there were hemorrhages between the uriniferous tubules of the cortex, within the glomeruli, within the walls of the afferent and efferent vessels of the glomeruli and fatty degeneration of the walls of the uriniferous tubules. Cicatricial tissue was quite common in the cortex of the kidney and blood cells could routinely be found in the hilus of the kidney.

The bladder was usually normal however a few animals had small granular cystic calculi present.

The adrenal gland showed degeneration and hemorrhage of the cortex.

Dietary Considerations

A disease identical or similar to the one being described has been observed previously and appeared to be dietary in origin. The three principal diets of the mink affected in this outbreak are listed below, together with the corrective diet:

Diets causing trouble	No. 1	No. 2	Corrective Diet
Cereal	5.8%	6.0%	3.0%
Milk powder	1.5%	1.5%	1.0%
Alfalfa meal	0.2%	0.2%	
Wheat germ	1.0%	1.0%	2.0%
Horsemeat (dry basis)	30.0%	30.5%	54.0%
Supplement	2.8%		
Fish	9.0%	10.0%	
Liver	10.0%	10.5%	2.0%
Tripe	8.0%	8.0%	
Tomato puree	1.5%	1.5%	2.0%
Water	30.2%	31.8%	33.5%
Liver meal			1.0%
Dried yeast			1.0%
Cod liver oil			.5%

As diets No. 1 and No. 2 appeared to be causing the trouble, the entire ranch was placed on the corrective diet and to this day they are still on it. The principal theory back of this change was to not only cut down on the concentration of the diet but to increase

the B_1 content of the ration. Diets No. 1 and No. 2 appeared to be too complicated and probably the protein content was too high.

Prognosis

A guarded prognosis was given, even though the liver has great regenerative capacity, much damage had been done to the hepatic cells and it was doubtful whether reversal could take place.

Transmission Experiments

In order to obtain animals that were in no way involved in this condition, we purchased animals from 10 different ranches on which the condition had not been observed. These were used only after the diet was checked in order to determine whether it was like the one that was causing the trouble.

Pooled material consisting of equal parts of brain, liver and spleen were injected subcutaneously in the axillary region of sixteen mink and eight ferrets. These animals were placed under close observation and daily temperatures were taken. No rise in temperature was observed and at the end of a two-week period, all 24 of the experimental animals were killed and necropsies held. Various tissues were cultured and routine laboratory examinations were made. The results were negative.

We endeavored to transmit the disease by natural methods. Normal mink were placed in pens in which a mink had died from this condition. At the end of a two-week period these animals were killed and routine laboratory examinations were conducted. Again the results were negative.

Tissue sections were made from all these animals but they appeared to be normal.

Summary

In 1943, 162 mink succumbed from this condition on one ranch and in 1944 the deaths numbered 390. Approximately one-third of the loss was males; two-thirds females. During the breeding season the loss was greatest in males; March being the month of greatest losses for both years.

Greatest loss occurred in mink that were one year of age or younger.

Cystic calculi were sometimes, but not routinely observed.

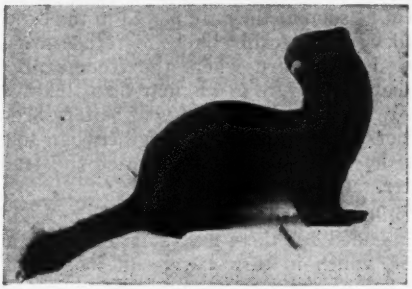
Ulceration of the gastric mucosa was observed in approximately 33% of the mink examined.

The seasons of the greatest loss relative to mink husbandry was during the mating season in males and during the whelping, nursing and weaning season in females.

Relating to weather conditions, the greatest losses occurred during cold weather, cold damp weather and extremely hot weather.

Observations of the animals in the yards showed little variation of symptoms of the condition, and lesions of the disease on necropsy were routinely identical, with slight variation in occasional cases.

Microscopic tissue studies revealed lesions of the disease in the heart, liver, lungs, kidneys, adrenals, stomach, central nervous system and the intestines. All animals showed practically the same lesions.



The outbreak occurred in mink that were fed 30% horsemeat, 5 to 6% cereal and various other ingredients that enriched the ration.

The disease could not be transmitted to normal mink either by pen transmission or by the injection of material from affected animals.

Discussion

This condition has assumed importance only within the last few years. Today the rancher is feeding more of a concentrated diet than heretofore; thereby getting farther away from the diet in the wild. This certainly has a bearing on this condition. Definite conclusions can be worked out only by further nutritional studies and chemical analyses.

Therapeutic measures persistently employed over a considerable period were of no avail; except that huge injections of thiamin hydrochloride seemed to prolong life somewhat.

Losses were checked only by the addition of filler products such as 10% apples, tripe, beets or any other bland food that would increase the bulk of the diet without increasing the food caloric value. Limiting the intake of food did not prove to be of value since the quality of the fur was injured and young mink died. Reducing the quality of the diet but not the quantity fed, proved to be the only solution to this problem. The theory back of this line of treatment is that the animal, by being maintained on a deficient diet will utilize the fat stored as lipoids in the liver.

Response from change of diet will be slow and the rancher must have full confidence in his veterinarian to carry out the recommendations.

Veterinary Problems in Poultry Production

By W. R. HINSHAW, D.V.M., Ph.D., Davis, California

Early brooder losses equivalent to those resulting from infections may be due to starvation caused by failure to teach chicks or poults to eat as soon as they are placed in the brooder. Poults are especially likely to refuse to eat if they do not learn where the feeders are immediately. Severe losses may also follow neglect to see that the openings in battery brooder feeders and waterers are large enough to permit the chicks or poults to reach the feed or water.

Failure to train the birds to use the feed that is intended for them may start them to eating litter, which in turn can result in starvation, because of the lack of nutrients in the litter. Litter eating can cause internal injuries from sharp coarse bits piercing the walls of the crop, gizzard and even the intestine. When sand is used for litter eating it may cause enteritis or "sand colic." Impactions of the crop and gizzard sometimes follow litter eating. Losses from these mechanical causes are preventable by proper management.

Ascites in Young Chicks and Young Poults

Ascites (anasarca, dropsy, watery belly) in both young chicks and poults has received considerable publicity during the past few years because of increased losses associated with this condition. Several causes have been determined and chief among these is the feeding of any sodium salt, even in small amounts. Older chicks and poults can tolerate considerable quantities of sodium chloride but when under one week of age as low as 2% in the ration, and smaller amounts in the drinking water, will cause marked edema of the tissues. Excess of salt in the ration is usually accidental and may be due to improper feed mixes, or poor screening which allows lumps to get into the mix. The addition of salt to rations which already contain it because of salted protein oncentrates has also been responsible for some cases.

A second cause of ascites is exposure to certain disinfectant fumes. Omphalitis resulting from infection during hatching or soon after being put into the brooder may also show similar edema. A correct diagnosis as to the cause of an outbreak of ascites in young birds requires a careful investigation of the existing conditions. Salt poisoning can often be determined by having an analysis made of the mash being fed at the time of the outbreak. The drinking water should not be overlooked as a possible source of the excess sodium, as a few cases have been reported where such water has been responsible. A history of the recent use of anthracene or similar sprays will aid in making a diagnoiss of acites due to disinfectant fumes.

Severe burns from anthracene oil sprays may result from placing chicks or poults in brooders too soon after the houses have been sprayed. Similar injuries have been reported by contact with oil and creosote from leaky oil or local burners. Such losses can be prevented by careful management. It is generally recommended that poults and chicks be kept out of brooders for two to three weeks after they are sprayed with anthracene oils and similar products.

Sulfaquinoxaline, a drug which has not yet been released for use for poultry diseases is showing promise as another remedy for coccidiosis, according to recent reports by Delaplane and his coworkers (*Science*, 107:196, 1948, and *Poultry Sci.* 27:169, 1948) and Peterson (*Am. J. Vet. Res.* 9:77, 1948).

This drug, according to the investigators, is toxic if given in doses greater than 0.1% in the mash for baby chicks, but is effective against both *Eimeria tenella* and *E. necatrix* infection when fed at levels as low as 0.125% in the mash. When fed at the rate of 0.05% intermittently, and 0.0125% continuously in the feed it was effective, and no toxicity was noted. Peterson found that the drug could be given in the drinking water and that 0.04% in water was equivalent to 0.1% in an all-mash ration, and that this amount could be given for three days without producing any toxic effects.

Because this drug has proved effective for the control of the two types of coccidiosis mentioned, it will no doubt be made available to veterinarians soon, along with the several other sulfonamides now available. Time will tell which one will prove the most effective for general use. Sulfaquinoxaline was first used by Delaplane (*Am. J. Vet. Res.* 6:207, 1945) in treatment of chronic fowl cholera in chickens.

Clinical Reports

Diabetes Mellitus in a Dog

A female terrier was presented for treatment with the following history. About two weeks previously, this animal had shown a tendency to laziness, at the same time she began to drink large quantities of water and excrete large quantities of urine. The hair had become sparse all over the body and completely denuded in some areas. One eye was completely keratinized. The dog showed an inclination towards being a little stupid and didn't move much. She had lost greatly in flesh and had become "pot-bellied." A tentative diagnosis of diabetes was made pending a urinalysis. The following morning the urine showed the following: S. gravity, 1.027; albumin, trace; sugar, 3 plus; acetone, positive; reaction, acid.

On the basis of the above, a diagnosis of diabetes mellitus was made. Unfortunately the owner could not afford a follow through on insulin and insisted upon euthanasia.

MARTIN G. LORBER, D.V.M.

Winston-Salem, N. C.

Prolapse of the Bladder in a Cow

February 23, 1948, I was called out to see a cow that according to the owner had "its womb sticking out of its body." On arrival at the farm a quick examination showed that instead of the uterus it was the bladder that was prolapsed. The cow had aborted a seven-month fetus.

A vaginal examination showed that the cervix was tightly closed with a heavy white mucoid discharge in the region of the cervix. The bladder with its covering about the size of a volley ball protruded along with the floor of the vagina. It was tensely engorged.

The protruding organs were well washed with a solution of saponated cresol and a sterile 3-inch, 14-gauge needle was passed into the bladder through the vaginal wall and about two pints of clear urine was removed. Also by judiciously lifting and squeezing the bladder another pint or so of urine was removed. By this time the bladder and vaginal wall were easily replaced in their normal position. I intended to catheterize the remaining urine and possibly inject a 1% solution of procaine into the bladder via the urethra, but did not have the necessary equipment with me at the time, so I made arrangements to return later that afternoon.

Upon my return, I found that the organs were still in place, so I just inserted a catheter and siphoned off another pint or so of urine, which was slightly turgid and blood stained. Optimistically I decided not to inject the procaine and not to insert any retaining sutures.

The next morning I was called and informed that the cow was in the same condition as when I was first called. When I reached the farm, the identical situation was presented except that the portion of vagina covering the prolapsed organ was tremendously engorged and slightly lacerated.

After washing the area the catheter was again inserted and a few pints of turgid, bloody, foul smelling urine was removed. This time after the organs were replaced I took a few retention sutures in the vulva. I also left methanimine 60 grain tablets to be given three times daily. The temperature was normal.

The sutures were removed two days later and the organs remained where nature intended them. The fact that struck me as being of particular interest was that there was no rupture in the vaginal wall so that at all times the bladder was completely covered by the vagina and the only way direct contact could be made with the bladder was by puncturing with a sterile needle or *via* catheter.

Frank refers to this type of prolapse of the floor of the vagina and the bladder as a vaginal cystocele, and remarks that it is mostly seen in pregnant cows and ewes and rarely post partum.

EDWIN E. EPSTEIN, D.V.M.

Sedalia, Mo.

Sporadic Occurrence of Malignant Edema in Swine

December 9, 1947, we were called out to do an autopsy on two heavy, fattening hogs that had died suddenly. The two animals were still warm when we arrived at the farm. We felt sure that if there were anything to be seen in the internal organs, it would not be obscured by post-mortem autolysis in these carcasses.

The only history available was that the animals were well and ate heartily in the morning. When the farmer went by their pen, about noon, they were both dead.

The necropsy disclosed the following:

There were no external wounds on the carcasses. However, in Pig No. 1, the axillary region was of a greenish black irridescent color. In Pig. No. 2, the same discoloration was evident in the groin and axillary regions. Crepitation could be felt in the area of discoloration.

The intestinal tracts showed no visible lesions. However, in spite of the fact that no ingesta was present, they were full of gas. The lungs showed evidence of rapid blood hemolysis and were dark greenish black and emphysematous. The pericardial sacs contained dark reddish-colored fluid. The pericardium was black, as seen in bloody inhibition. The myocardium was soft and friable, and there was little blood coagulation in the atria.

In Hog No. 1, the diaphragm was blackish green and showed muscular degeneration. This is a typical post-mortem lesion, as described by Hutyra & Marek. In both animals, the liver was bright green, having small bullae under the capsule which contained gas. The capsule did not peel. The liver tissue was soft and friable. There was slight inflammation of the gall bladder, and the bile was viscid. The spleen was slightly enlarged, and the medulla was of a soft, jelly-like consistency. There was a slight greenish color in the kidney, but no gross pathological changes were visible. The bladder was normal.

In the areas that showed the external discoloration, the subcutaneous tissue was black, the lymph glands were enlarged and hemorrhagic, and the entire area was emphysematous. There was a butyric acid-like odor emanating from the entire carcass.

Bacteriological examination showed gram-positive organisms with terminal spores. They did not culture on ordinary media, and we did not have the facilities for anaerobic culturing. Specimens of tissue from the lungs, heart, kidney, and liver were sent to a laboratory for study, but were useless because they decomposed so rapidly.

Conclusion.—The only explanation regarding the pathogenesis of these cases is that *Clostridium septicum*, which is a soil anaerobe, entered the digestive tract, invaded the lymphatics and portal circulation, and became localized, chiefly in muscular and subcutaneous tissue, soon setting up generalized septicemia.

Due to the rapidity of the disease, odor, rapid decomposition, nature of the organism, the presence of large amounts of gas, and the fact that no other animals in the drove were affected, we believe this to have been an outbreak of malignant edema in swine. It has been reported only a few times in this country, hence this report.

MARTIN LITWACK, D.V.M.
Fuquay Springs, N. C.

An Apparently Sexless Pig

An abnormal pig, apparently sexless, was examined recently in the laboratories of the Department of Veterinary Science at the University of Arkansas.

The pig was a purebred Chester White, approximately 12% inbred; the greatgrandsire on one side of the pedigree appeared as the grandsire on the other side.

All feet were abnormal. The usual number of toes was present, but with two exceptions the hoofs were vestigial. Two claws, each on a different foot, were abnormally long, apparently from disuse.

There were no recognizable external sex organs. At the umbilicus there was a small rounded projection of skin which may have been a vestigial prepuce. This structure had a small fibrous core directed vertically toward the abdominal wall which may have been either a vestigial penis or a remnant of the umbilical cord. It could not be dissected free from fat and fibrous tissue, therefore the structure could not be definitely determined.

The urine was voided through an orifice less than three millimeters in diameter which

was located just below the anus. This orifice was so small as to escape detection except when the pig was urinating or upon close examination. There was no indication of a vulva or a vagina.

The anus was large and the rectum slightly prolapsed. The abdominal viscera were searched carefully for vestiges of uterus, ovaries and testicles. None were found. There were no *ducti deferentia* passing through either of the inguinal canals and no visible scrotal pouches. An apparently normal cremaster muscle passed through each inguinal canal.

The pig was in good health, but had considerable difficulty moving about. When killed it was about five months old and weighed 83 pounds, live weight.

Since this pig is the most nearly sexless animal we have ever observed, we wish to call it to the attention of other veterinarians. We will appreciate their comments.

JOHN R. FENYK,
Associate Professor Bacteriology and Veterinary Science.
EDWARD CROOK,
Assistant Professor Bacteriology and Veterinary Science.
University of Arkansas, College of Agriculture, Fayetteville, Ark.

Choke Relieved Under General Anesthesia

The writer was called to see a Guernsey cow, three years of age that the owner said was choked. On first examination she was found to be restless, moderately bloated, and salivating profusely. A round hard object could be felt in the esophagus midway between the pharynx and the thoracic inlet.

A fruitless attempt was made to push the obstruction down with a stomach tube. Next an attempt was made to force the object, which was easily movable, up to the pharynx. By using one hand on each side of the neck, it could be forced to within six to eight inches of the pharynx. When that point was reached the cow would make strong swallowing efforts and throw herself about violently, causing all gains to be lost.

After several recurrences of this, it was decided to give her a general anesthetic. Approximately 700cc of 7% chloral hydrate, in 14% solution of magnesium sulfate was injected intravenously. By that time, the bloat in the cow, had progressed to a point, where breathing was impaired. A small horse trocar was inserted in the rumen and the gas released.

Because of the possibility that a pneumonia would result from the inhalation of saliva, care was taken to prop the cow up on her sternum while she was unconscious.

I then inserted my hand into the pharynx while an assistant forced the lodged object to where it could be grasped in the fingers. This was relatively simple once the swallowing reflex was obliterated. A very hard pear was found to be the offending obstruction.

Recovery of the cow was uneventful.

GEORGE SHINDEL, D.V.M.
Charleston, Ill.

This monster was the progeny of a Jersey cow and a Brahma bull. The cow had been in unsuccessful labor six hours when I was called. The calf was dead and delivery was effected without difficulty.

As shown in the illustration there was no mauddible. The ears were set much lower than normal and the tips were joined under the neck. The maxillary teeth were normal, except that the arcades were only an inch apart.

The mandible without teeth, the hyoid bone and a rudimentary tongue and larynx are contained in the enlargement which is shown just below the head.

Except for the head the calf was normal. The cow had two normal calves before this one. She had been on mineral depleted pasture but had access to a mineral supplement.—R. H. Hartman, D.V.M., Victoria, Texas.

According to Dr. L. E. Card, University of Illinois, a hen laying 140 two-ounce eggs per year requires for egg-laying alone about 20 pounds of dry feed, (or one pound for each seven eggs) beyond her other natural requirements. The number of eggs laid indicate how much extra feed should be furnished to keep up the particular production.

An ingenious method for computing the total feed for a laying hen is suggested by Doctor Card as follows:

Take the weight of the hen, multiply by eight, add 25. Divide the total number of eggs the hen lays by seven and add this figure to the first total for the feed required—thus, a five-pound hen laying 105 eggs per year would require 80 pounds of feed.

Abstracts

Efficacy of the Rapid Agglutination Test for Pullorum Disease

The author[19] has studied several methods of making agglutination tests for pullorum disease, namely, (1) the whole blood plate test; (2) the serum plate test; (3) the tube agglutination test. These tests were carried out under the usual conditions. The author concludes that the tube test is preferable to the others, giving the most reliable results. The whole blood plate test is quite reliable when performed at a temperature of 30°C. However, one has to reckon with false results if the test is performed at lower temperatures or if it is carried out in the presence of a great deal of dust. This method is reliable only in the hands of a competent research worker. In the hands of laymen it is unreliable. The serum rapid agglutination method is too inaccurate.

Streptomycin Therapy in Tuberculosis

A specific drug treatment for tuberculosis had long been sought—unsuccessfully. The introduction of the sulfonamides a little more than a decade ago and soon afterward various effective antibiotic agents, gave a tremendous stimulus to this search which is still being prosecuted with great energy and earnestness. As a result of recent research three sulfone compounds—promin, diasone, and promizole*—have been discovered to have a capacity to suppress tuberculosis in experimental animals and to have value in the treatment of the disease in man.

In an investigation of the effect of all known antibiotic agents on *M. tuberculosis in vitro* several were found that were antagonistic to it, but to date only streptomycin has demonstrated effectiveness against tuberculous infections. Feldman, and associates, has led in the study of the use of streptomycin in human and animal tuberculosis and has contributed articles on the subject annually or more frequently since 1944. His most recent publication,[8] reviews the work of himself and others in this field. He regards streptomycin as a valuable addition to the therapy of tuberculosis. Of course, it has limitations; one of them being the tendency of chronic tuberculosis to inflict irreversible pathologic changes in organs attacked. In acute miliary tuberculosis and meningeal tuberculosis, two forms causing heretofore practically 100% mortality, streptomycin has shown a remarkable ability to arrest the disease and apparently to cure it.

Tapeworm of Cats

Two new hosts of the cysticercus stage of *Taenia taeniaeformis* are the mice *Mus spicilegue* and *Apodermus flavicollis*. The author[14] also states that the morphology of the *Taenia taeniaeformis* and *Taenia infantis* are so similar that they may be the same.

More By-Products of Meat Packing Essential

The small abattoirs have a splendid opportunity[15] to increase their operating profits, lower the cost of meats and at the same time render a vital service to humanity by improving known by-products and providing a wider field for their application and developing substances now confined to the research laboratory.

By-products already developed to the point of practical utilization have a value of $25 per 1000-pound steer and the surface has barely been scratched in the development of by-products. Among the possibilities, already known, are thiouricil, thyroxin, thyro-protein and 20 amino-acids, the serum and globulin of the blood and antibodies all have uses but are mainly wasted.

The demand for insulin is great and increasing all the time. The time may come some day when it may be necessary to require of everyone who slaughters an animal that the pancreas be saved.

There is great waste in the utilization of fats, oils and greases by separating the fatty acids from glycerine and making soap. Many of the fatty acids are important to industry to separate low phosphate ores, as wetting agents and detergents in a great variety of chemical compounds.

Think of the enormous loss on the sale of hides due to grub or warble damage and yet that is easily preventable at no great cost. Tankage is not nearly as good as the industry can make. The high temperature at which it is processed destroys much of the vitamin B

19 Shumann, Professor, Doctor. How effective is the rapid agglutination test as a means of eradicating pullorum disease. Tierzliche Rundschau, No. 1, 2. 1943.

8 Feldman, Wm. H., and Hinshaw, H. Corwin. Streptomycin: a valuable anti-tuberculosis agent. *Brit. Med. J.*, No. 4541, pp. 87-92 (Jan. 17), 1948.

*The same compounds have displaced chaulmoogra oil in the treatment of leprosy.

14 Manheim, D. H. Contribution to the biology and the spreading of tapeworm in cats. Tierzliche Rundschau, No. 2, 1943.

15 Hart, George H. By-product utilization in the meat packing industry has barely been touched. Nat'l Provisioner 111:8, pp. 31-32. Feb. 21, 1948.

complex, the most valuable element in tankage, which is to be used for sheep, pig, and poultry feeding.

One of the great waste products is rumen contents. This is just about the richest product we have in vitamin B complex. It should be saved for pig and poultry feeding.

Study of Malignant-Catarrhal Fever in Cattle

The author[16] made a clinical, histopathological and cultural study of 18 cases of malignant catarrhal fever occurring in 14 herds of cattle in a single community in Ohio.

"Malignant catarrhal fever is an infectious, noncontagious, sporadic, highly fatal disease of cattle. Since the successful transmission of the disease by blood inoculation by Goetze and Liess, the etiologic agent has been thought to be a filterable virus. However, their filtration experiments and inoculations with blood plasma gave only negative results. Others were able to produce the disease in cattle by intravenous and subcutaneous inoculation of whole blood, but filtrates of such blood were not infective. No microorganisms could be demonstrated in the whole blood used for inoculation.

"Since cell inclusions are found in many virus diseases, a detailed search was made for their presence in malignant catarrhal fever. Of 18 cases of this disease occurring in one community, a detailed study of the pathologic changes was made in 3. This search revealed inclusion bodies in numerous tissues in all cases. The finding of these cytoplasmic cell inclusions in these cases should help establish the viral causation. Demonstration of inclusions may become a laboratory procedure which will aid in a positive diagnosis of this disease."

Symptoms.—The history and symptoms of all cases were similar. Animals of both sexes and ages from 10-month-old calves to mature animals were affected. The course varied from five to 14 days, and only two of 18 affected animals recovered.

"Excessive lacrimation, congestion of the sclera and conjunctiva, extreme dejection, dysphagia, dyspnea, and a temperature of 106°F. to 108°F. were noted on the first day. Later, cloudiness of the cornea occurred, as well as excessive salivation, with papule and vesicle formation on the muzzle, skin, and buccal, labial, gingival, and pharyngeal mucosa. The serous inflammation of the oral, nasal, and vaginal mucosa changed to sero-catarrhal, then catarrhal or croupous and, finally there were patches of epithelial excoriation from the muzzle and from the labial, pharyngeal and gingival regions. A fetid odor was emitted from the mouth and nostrils due to necrosis of the muzzle and mucous membranes.

"The vesicles in the skin ruptured, leaving moist areas, followed by drying of the serous fluid and epithelium, forming parchment-like crusts in the hair. Near the termination of the disease, the corium of the horns became detached from the corneal processes when bumped or grasped.

"*Lesions.*—The anatomic diagnosis included: papular and vesicular dermatitis, especially pronounced on the withers, forearms, scrotum, and testes; easy detachment of the corium of the horns from the cornual processes; serous, sero-hemorrhagic, croupous and diphtheritic stomatitis, pharyngitis, rhinitis and vaginitis; swollen submaxillary and anterior cervical lymph glands, and conjunctivitis. The corneas were opaque and more than twice as thick as is normal."

16 The pathology of malignant catarrhal fever—bovine epitheliosis. Goss, L. S., Cole, C. R., and Kissling, R. E., Am. J. of Pathology 23:5, pp. 837-841 (September) 1946.

Methods of Increasing Fertility in Farm Animals

Lowered fertility in animals has not been given adequate study and it is difficult to discuss a subject about which we have so many half-truths and so few facts.[17] Formerly irregular breeding and failure to reproduce was thought to be due mainly to infection and in many herds and individuals such proved to be true.

However, it has become abundantly evident there are other important causes of infertility in farm animals—heredity, endocrine imbalance, vitamin and mineral deficiencies and the burden of heavy lactation, etc. The mechanism by which these factors work is not clearly understood.

An outstanding fact is, some cases are pathological and hopeless. Such cases should be definitely determined by the clinician and eliminated from consideration for treatment. In another large group little or nothing can be found by clinical examination to account for sterility. In such animals there is a temptation to try everything in the hope something will work. Chemicals, minerals, ascorbic acid, vitamin A, chlorobutanol, calcium, cobalt, manganese, phosphorus, and various hormones have been reported to be useful in certain areas and certain animals. It is doubtful that the results of this trial and error treatment justify the expense. The use of hormones in particular has been an expensive experiment in large animals.

17 Fincher, M. G., Methods of increasing fertility in domestic animals. Transactions of the American Society for the Study of Sterility. 1947.

Heredity plays an important part in infertility. Certain animals including 90% or more of heifers twin to a bull, are permanently sterile because of undeveloped internal reproductuve organs. Occasional single-birth heifers also, are essentially neuters because of undeveloped uterus and ovaries. In still another more numerous group the reproductive organs are hypoplastic. These may vary from slight hypoplasia interfering but little with breeding to complete and permanent sterility. It is seen in white heifer disease and in bulls in which one testicle (and sometimes both) is markedly undersized. Little is known about a third division of hereditary causes of low fertility but there is considerable clinical evidence that individuals and families in cattle possess less than average fertility and are readily affected by nutritional or other factors that tend to depress reproduction.

It is important that animals of the first group be recognized as young calves, that their owners may be spared the expense of raising them for dairy purposes. Such recognition is not difficult. An ordinary six-inch test tube, one-half inch in diameter, can be passed its full length into the vulva and vagina of a normal heifer calf, but only three to three-and-one-half inches into the genital tract of freemartin or other neuter.

Females affected with genital hypoplasia, usually cannot be recognized until they are large enough to permit rectal examination. In some otherwise normal appearing heifers the ovaries are absent or only vestigial.

All individuals and families of the foregoing types should be eliminated from the breeding herd. Hormone treatment or other therapy is contraindicated. It is only in individuals and herds belonging to fertile families that hormone, vitamin or other therapy is likely to be profitable economically.

Hypoplasia of the gonads in bulls has already been mentioned. In addition a large group of males have slight and temporary changes in the testes at times. During these changes their fertility varies greatly and ascorbic acid injections, feeding chlorobutanol, manganese and other attempts to correct the nutrition have been reported to have value. Large daily doses of vitamin A seems to have value in such cases.

High producing dairy cows, a few beef cows and some mares develop multiple follicular cysts in one or both ovaries. They seldom experience a normal estrual cycle or conceive until the condition is corrected.

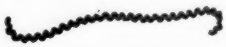
About 15% of the cases of cystic ovaries recover spontaneously. Rupturing the cysts manually is often unsatisfactory as a treatment. A limited experience with hormone treatment indicates approximately an 80% recovery from this type of therapy.

The author includes in the article an excellent review of the literature on the subject of infertility in cattle and its treatment. Farm animals other than cattle are mentioned only incidentally.

Canine Leptospirosis

Canine leptospirosis is of world wide distribution. It is not uncommon in this country. In the author's[18] opinion, the true incidence will not be known until there is wider appreciation of its prevalence and marked improvement in diagnostic methods.

Only recently has this disease come to be recognized as a health-hazard of man, who



Leptospira

Leptospira, genus of the order of Spirochaetales of the family Spirochaetaceae, are thin spiral organisms, flagellated at the extremities, one or both of which are bent back like a hook. L. canicola causes an infection in dogs which is transmissible to man. L. icterohaemorrhagiae is responsible for Weil's disease in man

may be infected by his dog. Sixteen species of Leptospira have been described but only two of them—canicola and ictero-hemorrhagiae are known to occur in man and dogs in the United States. The latter is supposed to occur more frequently in man and the former more frequently in the dog. Only the *Leptospira icterohemorrhage* has been found in the rat. Forty per cent of these rodents are infected.

Irrespective of the species to which the infection is due, the onset of the disease is sudden. There is muscular soreness, nasal and ocular discharge and a temperature of 103° to 105° F. The respiration is quickened and the pulse rate accelerated, with anorexia and persistent nausea and thirst.

As the disease progresses the thirst increases and toxic symptoms develop. The gait becomes staggering, symptoms of nephritis (polyuria) appear, then uremia, foul breath and a blood-tinged diarrhea signalize the end.

Formerly mortality was near 100% but more recently has been lowered by penicillin and serum therapy with supportive treatment.

Diagnosis is made by clinical examination, an agglutination test, culturing the organism from the blood stream or inoculation (hamsters).

18 Randall, Raymond. Canine leptospirosis. University of Pennsylvania, Vet. Ext. Bul. No. 106 (April) 1947.